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Requestor's Name: Geetha Bansal Serial Number: 09/642,666

Date: Jan 24, 2002 Phone: 305-3955 Art Unit: 1642

Search Topic:
Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

* This is a copy of the search performed on 2/4/02. I don't know what happened to the original Search report.

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PTO-1590 (9-90)

[redacted] STN sequence search

Bansal 09/642,660

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     FILE 'HCAPLUS' ENTERED AT 13:02:23 ON 04 FEB 2002
L2       130972 S FUSION OR CHIMERIC
L3           94 S L1
L4         3534 S LINKER?
L5            2 S L2 AND L3
L6            1 S L4 AND L3
L7            2 S L5 OR L6
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FILE 'REGISTRY' ENTERED AT 13:03:08 ON 04 FEB 2002
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STRUCTURE FILE UPDATES:     1 FEB 2002  HIGHEST RN 389104-08-9
DICTIONARY FILE UPDATES:    1 FEB 2002  HIGHEST RN 389104-08-9

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

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  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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incorporating CAS Registry Numbers with the P indicator between 12/27/01
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worldwide, or send an e-mail to help@cas.org for further assistance or to
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=> d qeu l21

L21 NOT FOUND

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L1          102 SEA FILE=REGISTRY ABB=ON  GSLGGS|GGGTSG/SQSP


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FILE LAST UPDATED: 30 Jan 2002 (20020130/ED)

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L5 2 S L2 AND L3
L6 1 S L4 AND L3
L7 2 S L5 OR L6

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FILE 'HCAPLUS' ENTERED AT 13:03:14 ON 04 FEB 2002

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L7 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
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DOCUMENT NUMBER: 135:268240
TITLE: Secreted and transmembrane polypeptides and human nucleic acids encoding them that are overexpressed in cancerous tissues
INVENTOR(S): Baker, Kevin P.; Chen, Jian; Desnoyers, Luc; Goddard, Audrey; Godowski, Paul J.; Gurney, Austin L.; Pan, James; Smith, Victoria; Watanabe, Colin K.; Wood, William I.; Zhang, Zemin
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 774 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 62
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

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WO	1999-US12252	W	19990602
US	1999-138166	P	19990608
US	1999-139695	P	19990615
US	1999-140650	P	19990622
US	1999-141037	P	19990623
US	1999-143048	P	19990707
US	1999-144732	P	19990720
US	1999-144758	P	19990720
US	1999-144791	P	19990720
US	1999-145070	P	19990720
US	1999-145698	P	19990726
US	1999-146222	P	19990728
US	1999-146970	P	19990803
US	1999-149396	P	19990817
WO	1999-US20111	W	19990901
WO	1999-US20594	W	19990908
WO	1999-US20944	W	19990913
WO	1999-US21090	W	19990915
WO	1999-US21547	W	19990915
WO	1999-US23089	W	19991005
US	1999-158663	P	19991008
US	1999-162506		19991029
WO	1999-US28214		19991129

WO	1999-US28313		19991130
WO	1999-US28409		19991130
WO	1999-US28301		19991201
WO	1999-US28634		19991201
WO	1999-US28551		19991202
WO	1999-US28564		19991202
WO	1999-US28565		19991202
US	1999-169495	P	19991207
US	1999-170262	P	19991209
WO	1999-US30095		19991216
WO	1999-US30911	A	19991220
WO	1999-US30999		19991220
US	1999-172096	P	19991223
WO	1999-US31274		19991230
WO	2000-US219		20000105
WO	2000-US277		20000106
WO	2000-US376	A	20000106
US	2000-175481	P	20000111
WO	2000-US3565	A	20000211
WO	2000-US4341	A	20000218
WO	2000-US4342	A	20000218
WO	2000-US4414	A	20000222
WO	2000-US4914	A	20000224
WO	2000-US5004	A	20000224
WO	2000-US6319	A	20000310
WO	2000-US7377	W	20000320
WO	2000-US7532	A	20000321
US	2000-213087	P	20000622
US	2000-219556	P	20000720
US	2000-220585	P	20000725
US	2000-220605	P	20000725
US	2000-220607	P	20000725
US	2000-220624	P	20000725
US	2000-220638	P	20000725
US	2000-220664	P	20000725
US	2000-220666	P	20000725
US	2000-220893	P	20000726
US	2000-222425	P	20000801
WO	2000-US22031	W	20000811
US	2000-227133	P	20000822
WO	2000-US23522	W	20000823
US	2000-242837	P	20001024
WO	2000-US30873	W	20001110
US	2000-253646	P	20001128
US	2000-747259	A	20001220
WO	2001-US6520	W	20010228

AB The present invention is directed to novel polypeptides and to nucleic acid mols. encoding those polypeptides. Thus, 305 cDNAs encoding human secreted or transmembrane proteins were identified by extracellular domain homol. screening, amylase screening, and signal algorithm anal. These transcripts for these proteins are overexpressed in various cancerous tissues, including adrenal, lung, colon, breast, prostate, rectal, cervical, and liver tumors. Certain of the proteins stimulate release of tumor necrosis factor-.alpha. from human blood, and also stimulate proliferation or differentiation of chondrocytes. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

IC ICM C12N015-12
ICS C12N015-62; C07K014-47; C07K014-705; C07K016-18; G01N033-53; C12Q001-68
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 6, 13, 14
IT Antibodies
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**chimeric**; secreted and transmembrane polypeptides and human nucleic acids encoding them that are overexpressed in cancerous tissues)
IT **Fusion** proteins (**chimeric** proteins)
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(secreted and transmembrane polypeptides and human nucleic acids encoding them that are overexpressed in cancerous tissues)
IT 151185-21-6 160575-51-9 185229-04-3 200145-68-2 202669-30-5
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208668-52-4 208668-58-0 209209-94-9 209334-83-8 209859-57-4
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213474-05-6 214684-34-1 217795-43-2 217795-45-4 217795-48-7
218438-77-8 218948-50-6 219709-98-5 220104-93-8
220483-73-8 220710-70-3 220793-26-0 221079-13-6 221216-74-6
221266-03-1 221369-75-1 221369-76-2 221369-81-9 221455-95-4
221877-69-6 221877-79-8 221877-95-8 221878-41-7 221879-04-5
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312334-32-0 312334-52-4 313408-13-8 314326-52-8 314326-55-1
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329286-29-5 329286-30-8 329799-91-9 329799-99-7
RL: ANT (Analyte); BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(amino acid sequence; secreted and transmembrane polypeptides and human nucleic acids encoding them that are overexpressed in cancerous tissues)

L7 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:769010 HCAPLUS
DOCUMENT NUMBER: 133:334053
TITLE: Preparation and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig molecular complexes to analyze and modulate antigen-specific T cell-dependent immune responses
INVENTOR(S): Schneck, Jonathan; O'Herrin, Sean; Lebowitz, Michael S.; Hamad, Abdel
PATENT ASSIGNEE(S): The Johns Hopkins University, USA
SOURCE: U.S., 41 pp., Cont.-in-part of U.S. 6,015,884.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6140113	A	20001031	US 1998-63276	19980421
US 6015884	A	20000118	US 1997-828712	19970328
US 2002006903	A1	20020117	US 2001-789720	20010222

PRIORITY APPLN. INFO.:
US 1996-14367 P 19960328
US 1997-828712 A2 19970328
US 1997-58573 P 19970911
US 1998-82538 P 19980421
US 1998-150622 A3 19980910

AB Sol. multivalent chimeric TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses are described. The mol. complexes comprise extracellular domains of transmembrane heterodimeric proteins, particularly T cell receptor and major histocompatibility complex proteins, which are covalently linked to the heavy and light chains of Ig mols. to provide sol. multivalent mol. complexes with high affinity for their cognate ligands. Studies of the affinity and binding specificity of these multivalent chimeric TCR/Ig or MHC/Ig mols. to antigenic peptides are reported. The mol. complexes can be used, inter alia, to detect and regulate antigen-specific T cells and as therapeutic agents for treating disorders involving immune system regulation, such as allergies, autoimmune diseases, tumors, infections, and transplant rejection.

IC ICM C12N015-63
ICS C12N015-09; C12N005-10; C12N015-66; C07H021-00
NCL 435320100
CC 15-3 (Immunochemistry)
Section cross-reference(s): 3, 6, 13
ST TCR receptor Ig **fusion** protein immune response modulation; MHC class II Ig **fusion** protein immune response modulation
IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic

use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(G1, **fusion** products, with TCR or MHC; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(I-Ek, **fusion** products, with IgG1; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(MHC (major histocompatibility complex), class II, **fusion** products, with IgG1; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(MHC (major histocompatibility complex), class II, .alpha., **fusion** products with IgG1; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(MHC (major histocompatibility complex), class II, .beta., **fusion** products with IgG1; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(T-cell-dependent antigens; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT Ligands
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(cognate; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT Protein motifs
(extracellular domain; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT Immunoglobulins

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(heavy chains, **fusion** products with TCR or MHC; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT Autoimmune disease
Disease, animal
Neoplasm
(involving immune system, therapy; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(light chains, **fusion** products with TCR or MHC; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(light chains, .kappa., **fusion** products with TCR or MHC; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT Peptides, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**linker**, between Ig light chain and extracellular domain of TCR or MHC; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT Infection
(microbial, therapy; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT **Fusion** proteins (**chimeric** proteins)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(of TCR/Ig or MHC/Ig; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT Immunity
Molecular cloning
Protein engineering
(prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT Allergy
Transplant rejection
(therapy; prepn. and characterization of sol. multivalent

chimeric TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT TCR (T cell receptors)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(.alpha., **fusion** products, with IgG1; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT TCR (T cell receptors)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(.beta., **fusion** products, with IgG1; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT 127902-44-7 132326-74-0 142606-55-1 152338-19-7 159646-83-0 178561-37-0 181272-91-3 181309-90-0 198695-89-5
RL: PRP (Properties)
(Unclaimed; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT **303983-56-4 303983-57-5**
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence of peptide **linker**; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

IT 303815-90-9, 1: PN: US6140113 SEQID: 1 unclaimed DNA 303815-91-0, 2: PN: US6140113 SEQID: 2 unclaimed DNA 303815-92-1, 3: PN: US6140113 SEQID: 3 unclaimed DNA 303815-93-2, 4: PN: US6140113 SEQID: 4 unclaimed DNA 303815-94-3, 5: PN: US6140113 SEQID: 5 unclaimed DNA 303815-95-4, 6: PN: US6140113 SEQID: 6 unclaimed DNA 303815-96-5, 7: PN: US6140113 SEQID: 7 unclaimed DNA 303815-97-6, 8: PN: US6140113 SEQID: 8 unclaimed DNA 303815-98-7, 9: PN: US6140113 SEQID: 9 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; prepn. and characterization of sol. multivalent **chimeric** TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> select hit rn l7 1-2
E1 THROUGH E3 ASSIGNED

=> fil reg
FILE 'REGISTRY' ENTERED AT 13:05:44 ON 04 FEB 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 1 FEB 2002 HIGHEST RN 389104-08-9
DICTIONARY FILE UPDATES: 1 FEB 2002 HIGHEST RN 389104-08-9

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator between 12/27/01 and 1/23/02, are encouraged to re-run these strategies. Contact the CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698, worldwide, or send an e-mail to help@cas.org for further assistance or to receive a credit for any duplicate searches.

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               (218438-77-8/RN)
             1 303983-56-4/BI
               (303983-56-4/RN)
             1 303983-57-5/BI
               (303983-57-5/RN)
L8           3 (218438-77-8/BI OR 303983-56-4/BI OR 303983-57-5/BI)

=> s l1 and l8
L9           3 L1 AND L8

=> d sqide3 1-3

L9   ANSWER 1 OF 3  REGISTRY  COPYRIGHT 2002 ACS
RN   303983-57-5  REGISTRY
CN   L-Serine, glycyl-L-seryl-L-leucylglycylglycyl- (9CI)  (CA INDEX NAME)
FS   PROTEIN SEQUENCE; STEREOSEARCH
SQL  6

SEQ3     1 Gly-Ser-Leu-Gly-Gly-Ser
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MF   C18 H32 N6 O9
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL

Absolute stereochemistry.
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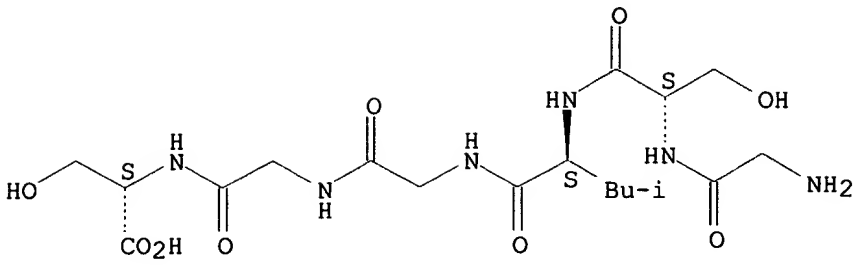

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L9 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2002 ACS
RN **303983-56-4** REGISTRY
CN Glycine, glycylglycylglycyl-L-threonyl-L-seryl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 6

SEQ3 1 Gly-Gly-Gly-Thr-Ser-Gly
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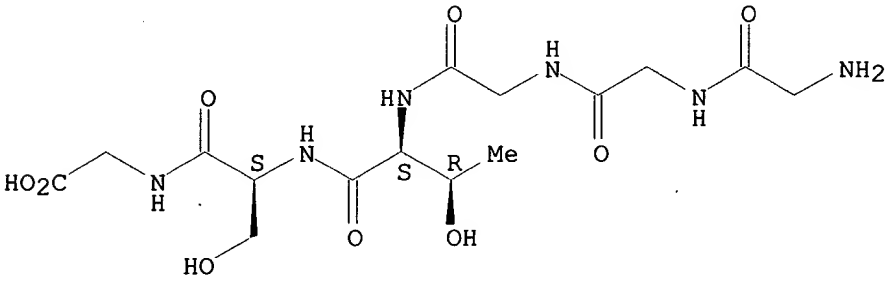
HITS AT: 1-6

MF C15 H26 N6 O9
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L9 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2002 ACS
RN **218438-77-8** REGISTRY
CN Protein LS170 (human clone 1355520IH) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 12: PN: WO0175068 SEQID: 62 claimed protein
CN 159: PN: WO0168848 FIG: 374 claimed protein
CN 1: PN: JP2001078772 SEQID: 1 claimed protein
CN 2492: PN: WO0153312 SEQID: 2866 claimed sequence
CN 6: PN: WO0008206 SEQID: 6 unclaimed protein
CN GenBank AB024937-derived protein GI 7415994
CN GenBank AF158745-derived protein GI 9081879
CN Protein (human clone 784CIF2B_769 precursor)
CN Protein (human clone IMAGE 255754 gene YH1)
CN Protein LUNX (lung-specific X protein) (human gene LUNX)

CN Protein LUNX (lung-specific X) (human lung gene LUNX)
CN Protein PRO1606 (human clone DNA76533-1689 precursor)
CN Secretory protein (human clone nh796_1 precursor)
FS PROTEIN SEQUENCE
SQL 256

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        31 Thr-Leu-Pro-Leu-Asn-Val-Asn-Pro-Ala-Leu-
        41 Pro-Leu-Ser-Pro-Thr-Gly-Leu-Ala-Gly-Ser-
        51 Leu-Thr-Asn-Ala-Leu-Ser-Asn-Gly-Leu-Leu-
        61 Ser-Gly-Gly-Leu-Leu-Gly-Ile-Leu-Glu-Asn-
        71 Leu-Pro-Leu-Leu-Asp-Ile-Leu-Lys-Pro-Gly-
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        81 Gly-Gly-Thr-Ser-Gly-Gly-Leu-Leu-Gly-Gly-
           === === === === ===
        91 Leu-Leu-Gly-Lys-Val-Thr-Ser-Val-Ile-Pro-
       101 Gly-Leu-Asn-Asn-Ile-Ile-Asp-Ile-Lys-Val-
       111 Thr-Asp-Pro-Gln-Leu-Leu-Glu-Leu-Gly-Leu-
       121 Val-Gln-Ser-Pro-Asp-Gly-His-Arg-Leu-Tyr-
       131 Val-Thr-Ile-Pro-Leu-Gly-Ile-Lys-Leu-Gln-
       141 Val-Asn-Thr-Pro-Leu-Val-Gly-Ala-Ser-Leu-
       151 Leu-Arg-Leu-Ala-Val-Lys-Leu-Asp-Ile-Thr-
       161 Ala-Glu-Ile-Leu-Ala-Val-Arg-Asp-Lys-Gln-
       171 Glu-Arg-Ile-His-Leu-Val-Leu-Gly-Asp-Cys-
       181 Thr-His-Ser-Pro-Gly-Ser-Leu-Gln-Ile-Ser-
       191 Leu-Leu-Asp-Gly-Leu-Gly-Pro-Leu-Pro-Ile-
       201 Gln-Gly-Leu-Leu-Asp-Ser-Leu-Thr-Gly-Ile-
       211 Leu-Asn-Lys-Val-Leu-Pro-Glu-Leu-Val-Gln-
       221 Gly-Asn-Val-Cys-Pro-Leu-Val-Asn-Glu-Val-
       231 Leu-Arg-Gly-Leu-Asp-Ile-Thr-Leu-Val-His-
       241 Asp-Ile-Val-Asn-Met-Leu-Ile-His-Gly-Leu-
       251 Gln-Phe-Val-Ile-Lys-Val
HITS AT:   80-85
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MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT
9 REFERENCES IN FILE CA (1967 TO DATE)
9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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=> d his

     (FILE 'HCAPLUS' ENTERED AT 12:18:04 ON 04 FEB 2002)
               DEL HIS Y
L1         17103 S FUSION (L) PROTEIN?
L2         10103 S CHIMER? (L) PROTEIN#
L3         18986 S L1 OR L2
L4        125398 S MOL? (L) COMPLEX?
L5            56 S L4 (L) L3
L6         76248 S IG OR IMMUNOGLOBULIN#
L7             6 S L5 AND L6
L8          4662 S MULTIVALENT OR HETERODIMER?
L9             3 S L5 AND L8
L10            6 S L7 OR L9
L11         2383 S L3 AND L6
L12        13933 S TCR OR T CELL RECEPTOR#
L13         5092 S L12 (L) ALPHA
L14        26924 S MHC OR HISTOCOMPATIBIL?
L15           32 S L11 AND L13
L16          123 S L11 AND L14
L17          143 S L15 OR L16
L18           11 S L17 AND L8
L19            1 S L18 AND (TRANSMEMB? OR TRANSMEMBRA?/AB)
L20        86274 S (IMMUNE OR IMMUNITY)
L21           16 S L17 AND (TRANSMEMB? OR TRANSMEMBRA?/AB)
L22        19756 S (MULTIVALEN? OR HETERODIMER?)/AB
L23           14 S L17 AND L22
L24           17 S L18 OR L23
L25           32 S L18 OR L19 OR L21 OR L23 OR L24
L26           12 S L25 AND L20
L27           16 S L26 OR L10
L28           16 S L25 AND (TRANSMEMB? OR TRANSMEMB?/AB)
L29         3534 S LINKER?
L30            8 S L17 AND L29
L31           23 S L30 OR L27
L32         7634 S IMMUNOMODUL?
L33            7 S L17 AND L32
L34           27 S L33 OR L31
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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 12:41:23 ON 04 FEB 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)
```



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FILE COVERS 1907 - 1 Feb 2002  VOL 136 ISS 6
FILE LAST UPDATED: 30 Jan 2002  (20020130/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the
CAS Registry Numbers that were added to the CAS files between 12/27/01
and 1/23/02.  As of 1/23/02, the situation has been resolved.  Searches
and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry
Numbers with the P indicator executed between 12/27/01 and 1/23/02 may
be incomplete.  See the NEWS message on this topic for more information.
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d his

     (FILE 'HCAPLUS' ENTERED AT 12:18:04 ON 04 FEB 2002)
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L1         17103 S FUSION (L) PROTEIN?
L2         10103 S CHIMER? (L) PROTEIN#
L3         18986 S L1 OR L2
L4        125398 S MOL? (L) COMPLEX?
L5            56 S L4 (L) L3
L6         76248 S IG OR IMMUNOGLOBULIN#
L7             6 S L5 AND L6
L8          4662 S MULTIVALENT OR HETERODIMER?
L9             3 S L5 AND L8
L10            6 S L7 OR L9
L11         2383 S L3 AND L6
L12        13933 S TCR OR T CELL RECEPTOR#
L13         5092 S L12 (L) ALPHA
L14        26924 S MHC OR HISTOCOMPATIBIL?
L15           32 S L11 AND L13
L16          123 S L11 AND L14
L17          143 S L15 OR L16
L18           11 S L17 AND L8
```

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L19           1 S L18 AND (TRANSMEMB? OR TRANSMEMBRA?/AB)
L20       86274 S (IMMUNE OR IMMUNITY)
L21          16 S L17 AND (TRANSMEMB? OR TRANSMEMBRA?/AB)
L22       19756 S (MULTIVALEN? OR HETERODIMER?)/AB
L23          14 S L17 AND L22
L24          17 S L18 OR L23
L25          32 S L18 OR L19 OR L21 OR L23 OR L24
L26          12 S L25 AND L20
L27          16 S L26 OR L10
L28          16 S L25 AND (TRANSMEMB? OR TRANSMEMB?/AB)
L29        3534 S LINKER?
L30           8 S L17 AND L29
L31          23 S L30 OR L27
L32        7634 S IMMUNOMODUL?
L33           7 S L17 AND L32
L34          27 S L33 OR L31

     FILE 'HCAPLUS' ENTERED AT 12:41:23 ON 04 FEB 2002

=> d .ca 1-27

L34  ANSWER 1 OF 27  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:10544  HCAPLUS
DOCUMENT NUMBER:          136:84694
TITLE:                    High throughput generation and screening of fully
                          human antibody repertoire in yeast
INVENTOR(S):              Zhu, Li; Hua, Shaobing Benjamin
PATENT ASSIGNEE(S):       Genetastix Corporation, USA
SOURCE:                   PCT Int. Appl., 251 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2002000729      A2   20020103       WO 2001-US20542  20010625
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
             UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                  US 2000-602373   A1 20000623
                                        US 2000-602972   A  20000623
                                        US 2000-602973   A1 20000623
                                        US 2000-603658   A1 20000623
                                        US 2000-603663   A1 20000623
```

AB Compns., kits and methods are provided for generating highly diverse libraries of proteins such as antibodies via homologous recombination in vivo, and screening these libraries against protein, peptide and nucleic acid targets using a two-hybrid method in yeast. The method for screening a library of tester fusion proteins against a target protein or peptide comprises: expressing a library of tester proteins in yeast cells, the tester fusion protein comprising a first polypeptide subunit whose sequence varies within the library, a second polypeptide subunit whose

sequence varies within the library independently of the first polypeptide, and a linker peptide which links the first and second polypeptide subunits; expressing one or more target fusion proteins in the yeast cells expressing the tester proteins, each of the target fusion proteins comprising a target peptide or protein; and selecting those yeast cells in which a reporter gene is expressed, the expression of the reporter gene being activated by binding of the tester fusion protein to the target fusion protein.

IC ICM C07K016-00
CC 15-3 (Immunochemistry)
Section cross-reference(s): 2, 3
IT Gene, animal
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); CPN (Combinatorial preparation); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(**Ig.**; high throughput generation and screening of fully human antibody repertoire in yeast)
IT **Histocompatibility** antigens
RL: BSU (Biological study, unclassified); CUS (Combinatorial use); BIOL (Biological study); CMBI (Combinatorial study); USES (Uses)
(**MHC** (major **histocompatibility** complex); high throughput generation and screening of fully human antibody repertoire in yeast)
IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); CPN (Combinatorial preparation); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); PRP (Properties); USES (Uses)
(heavy chains; high throughput generation and screening of fully human antibody repertoire in yeast)
IT Antibodies
Fusion proteins (chimeric proteins
)
Immunoglobulins
RL: BPN (Biosynthetic preparation); CPN (Combinatorial preparation); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); PRP (Properties); USES (Uses)
(high throughput generation and screening of fully human antibody repertoire in yeast)
IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); CPN (Combinatorial preparation); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); PRP (Properties); USES (Uses)
(light chains; high throughput generation and screening of fully human antibody repertoire in yeast)
IT Peptides, biological studies
RL: BSU (Biological study, unclassified); CUS (Combinatorial use); BIOL (Biological study); CMBI (Combinatorial study); USES (Uses)
(**linker**; high throughput generation and screening of fully human antibody repertoire in yeast)

L34 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:833384 HCAPLUS
DOCUMENT NUMBER: 135:370640
TITLE: Human monoclonal antibodies to dendritic cells
INVENTOR(S): Deo, Yashwant M.; Keler, Tibor
PATENT ASSIGNEE(S): Medarex, Inc., USA

SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085798	A2	20011115	WO 2001-US15114	20010508

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-203126 P 20000508
US 2000-230739 P 20000907

AB Isolated human monoclonal antibodies and antigen-binding portions thereof which specifically bind to dendritic cells are disclosed. Also disclosed are bispecifics, immunotoxins and antigen conjugates which include the antibodies or antibody portions. The human antibodies can be produced in a non-human transgenic animal, e.g. a transgenic mouse, capable of producing multiple isotypes of human monoclonal antibodies by undergoing V-D-J recombination and isotype switching. Also disclosed are pharmaceutical compns. comprising the human antibodies, non-human transgenic animals and hybridomas which produce the human antibodies. The invention also provides therapeutic and diagnostic methods for autoimmune diseases or graft vs. host diseases by using the human antibodies.

IC ICM C07K016-28
ICS C12N005-20; A01K067-027; C07K016-46; A61K039-395; A61K047-48; G01N033-569; G01N033-577; C12N015-63; A61K039-00; A61K039-02; A61K039-12; A61P031-00; A61P035-00; A61P037-00
CC 15-3 (Immunochemistry)
Section cross-reference(s): 3, 63

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A, secretory; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A1; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A2; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(D; bispecific human monoclonal antibodies to dendritic cells for

diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G1; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G2; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G3; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G4; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT Recombination, genetic
(**Ig** class switching; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Immunoglobulin** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(IgA, human; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Immunoglobulin** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(IgG type I, human; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(M; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Histocompatibility** antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**MHC** (major **histocompatibility** complex), class I; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Histocompatibility** antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**MHC** (major **histocompatibility** complex), class II; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT Animal virus
Antigen-presenting cell
Autoimmune disease
B cell (lymphocyte)
Bacteria (Eubacteria)
Cytolysis
DNA sequences
Dendritic cell
Genetic vectors
Hybridoma
Immunomodulators
Immunotherapy
Macaca irus
Microorganism
Molecular cloning
Pathogen
Protein sequences
(bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Fusion proteins** (**chimeric proteins**)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fragments; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heavy chains, variable; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Immunoglobulin** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(human; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and graft vs. host disease)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(light chains, variable; bispecific human monoclonal antibodies to dendritic cells for diagnosis and treatment of autoimmune disease and

graft vs. host disease)

L34 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:338706 HCAPLUS
DOCUMENT NUMBER: 134:363069
TITLE: Chimeric receptors using expanded primary signalling motifs for T cell activation
INVENTOR(S): Finney, Helene Margaret; Lawson, Alastair David Griffiths
PATENT ASSIGNEE(S): Celltech Chiroscience Limited, UK
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032867	A1	20010510	WO 2000-GB4193	20001101

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-25853 A 19991101

AB The invention relates to novel primary signaling motifs, which are based on consensus sequence of primary signalling motifs of Ig tyrosine receptor-based activation motifs (ITAMs): Y-X2-L/I-Xn-Y-X2-L/I, where n is 9 or greater. These novel motifs are extremely efficient at mediating immune cell signal transduction, particularly when incorporated in an intracellular signaling domain of a chimeric receptor. The use of such signalling mols. within chimeric receptor proteins allows one to tailor the level of intracellular signalling mediated by the chimeric receptor. Proteins contg., and nucleic acids encoding, such synthetic signalling mols. suitable for use in medicine, are described.

IC ICM C12N015-12
ICS C07K014-705; C12N015-62; C12N005-10; A61K038-17

CC 6-1 (General Biochemistry)
Section cross-reference(s): 3, 15

ST T cell activation expanded signalling motif **chimeric** receptor; **Ig** receptor signaling motif **fusion protein** signal transduction

IT Antigens
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(CD134, fusion products contg. signal transduction or **transmembrane** domain of; chimeric receptors using non-natural primary signalling motifs for T cell activation)

IT Glycoproteins, specific or class
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(CD40-L (antigen CD40 ligand), fusion products contg. signal transduction or **transmembrane** domain of; chimeric receptors using non-natural primary signalling motifs for T cell activation)

IT **Immunoglobulin** receptors

RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(FcR.beta., fusion products contg. signal transduction domain of; chimeric receptors using non-natural primary signalling motifs for T cell activation)

IT **Protein** motifs
(ITAM (**Ig** tyrosine receptor-based activation motifs); **chimeric** receptors using non-natural primary signalling motifs for T cell activation)

IT **Immunoglobulin** receptors
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(IgE type I, fusion products contg. signal transduction domain of; chimeric receptors using non-natural primary signalling motifs for T cell activation)

IT **Immunoglobulin** receptors
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(IgG type I, fusion products contg. signal transduction domain of; chimeric receptors using non-natural primary signalling motifs for T cell activation)

IT **Immunoglobulin** receptors
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(IgG type III, fusion products contg. signal transduction domain of; chimeric receptors using non-natural primary signalling motifs for T cell activation)

IT **Immunoglobulin** receptors
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(IgG, fusion products contg. signal transduction domain of; chimeric receptors using non-natural primary signalling motifs for T cell activation)

IT Gene therapy
(altering patterns of signal transduction in **immune** system; chimeric receptors using non-natural primary signalling motifs for T cell activation)

IT **Protein** motifs
(antibody-binding domain, in **chimeric** receptors; **chimeric** receptors using non-natural primary signalling motifs for T cell activation)

IT **Protein** motifs
(extracellular ligand-binding domain, in **chimeric** receptors; **chimeric** receptors using non-natural primary signalling motifs for T cell activation)

IT **Fusion proteins (chimeric proteins)**
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(for signal transduction; **chimeric** receptors using non-natural primary signalling motifs for T cell activation)

IT **Chimeric** gene
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(for synthetic signal transducing **fusion proteins**; **chimeric** receptors using non-natural primary signalling motifs for T cell activation)

IT **Immunoglobulins**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(fragments, Fab', as extracellular ligand-binding domain in chimeric

receptors; chimeric receptors using non-natural primary signalling motifs for T cell activation)

IT CD22 (antigen)
CD28 (antigen)
CD5 (antigen)
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(fusion products contg. signal transduction or **transmembrane** domain of; chimeric receptors using non-natural primary signalling motifs for T cell activation)

IT CD4 (antigen)
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(fusion products contg. **transmembrane** domain of; chimeric receptors using non-natural primary signalling motifs for T cell activation)

IT Apoptosis
(signal transduction **proteins** for induction by antigens of; **chimeric** receptors using non-natural primary signalling motifs for T cell activation)

IT Cytokines
Interleukin 2
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(signal transduction **proteins** for induction of release of; **chimeric** receptors using non-natural primary signalling motifs for T cell activation)

IT **Protein** motifs
(signaling motif in **chimeric** receptors; **chimeric** receptors using non-natural primary signalling motifs for T cell activation)

IT **Protein** motifs
(**transmembrane** domain, in **chimeric** receptors; **chimeric** receptors using non-natural primary signalling motifs for T cell activation)

IT TCR (T cell receptors)
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(.zeta. chain, fusion products contg. signal transduction ot **transmembrane** domain of; chimeric receptors using non-natural primary signalling motifs for T cell activation)

IT **TCR (T cell receptors)**
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(.**alpha**. chain, fusion products contg. signal **transmembrane** domain of; chimeric receptors using non-natural primary signalling motifs for T cell activation)

IT TCR (T cell receptors)
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(.beta. chain, fusion products contg. signal **transmembrane** domain of; chimeric receptors using non-natural primary signalling motifs for T cell activation)

IT CD3 (antigen)
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(.epsilon. chain, fusion products contg. signal transduction or **transmembrane** domain of; chimeric receptors using non-natural primary signalling motifs for T cell activation)

IT 339525-38-1
RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use);

BIOL (Biological study); PROC (Process); USES (Uses)
(**Ig** tyrosine receptor-based activation motifs (ITAMs); chimeric receptors using non-natural primary signalling motifs for T cell activation)
IT 339525-39-2 339525-73-4 339525-74-5 339525-75-6 339525-76-7
339525-77-8 339525-78-9 339525-79-0
RL: PRP (Properties)
(unclaimed **protein** sequence; **chimeric** receptors using expanded primary signalling motifs for T cell activation)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:881321 HCAPLUS
DOCUMENT NUMBER: 134:38630
TITLE: Streptavidin expressed gene fusions forming tetrameric complexes with therapeutic implications for adenocarcinomas and hematol. malignancies
INVENTOR(S): Goshorn, Stephen Charles; Graves, Scott Stoll; Schultz, Joanne Elaine; Lin, Yukang; Sanderson, James Allen; Reno, John M.
PATENT ASSIGNEE(S): Neorx Corp., USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075333	A1	20001214	WO 2000-US15595	20000605

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-137900 P 19990607
US 1999-168976 P 19991203

AB The present invention provides vectors for expressing genomic streptavidin fusion cassettes which include inducible promoters and various linkers and signal sequences. In the various embodiments, fusion proteins produced from these vectors are provided. In particular embodiments, fusion proteins comprising a single chain antibody (huNR-LU-10) and genomic streptavidin are provided as are vectors encoding the same. Also provided, are methods of using the fusion proteins of the present invention, and in particular, the use of scFvSA fusion proteins involving B9E9 as diagnostic markers or as a cell specific targeting agents. In addn. tetravalent antibodies that contact a fusion protin forming a tetrametric complex which may comprise a tumor cell surface-assocd. protein and a streptavidin portion capable of binding biotin and a biotinylated radionuclide contg. compd. A immunoreactivity assay is described in addn. to monitoring of blood clearance and tumor uptake of fusion proteins. Some adenocarcinomas and hematol. malignancies such as non-Hodgkin's lymphoma may be treated with these fusio-protein expressing vectors. This system offers the expression of a genomic streptavidin gene

fusion as a sol. protein into the periplasmic space of Escherichia coli where it undergoes spontaneous folding. This expression offers efficient protein folding where one does not need to purify and refold the protein expressed.

IC ICM C12N015-31
ICS C12N015-13; C12N015-62; C12N015-72; C12N001-21; C07K014-36; C07K016-28; A61K039-395; A61K047-48

CC 6-3 (General Biochemistry)
Section cross-reference(s): 15

ST fusion gene Streptavidin Biotin immunoassay vector adenocarcinoma hematol malignancy; periplasm expression fusion protein **Ig** Streptavidin immunoassay tumor therapy

IT Cell adhesion **molecules**
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(N-CAM, antibodies specific for **fusion protein** comprising; streptavidin expressed gene fusions forming tetrameric **complexes** with therapeutic implications for adenocarcinomas and hematol. malignancies)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fragments, single-chain Fv fragment; streptavidin expressed gene fusions forming tetrameric complexes with therapeutic implications for adenocarcinomas and hematol. malignancies)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(heavy chains, linker connecting variable light and heavy chains; streptavidin expressed gene fusions forming tetrameric complexes with therapeutic implications for adenocarcinomas and hematol. malignancies)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(light chains, linker connecting variable light and heavy chains; streptavidin expressed gene fusions forming tetrameric complexes with therapeutic implications for adenocarcinomas and hematol. malignancies)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:769010 HCAPLUS
DOCUMENT NUMBER: 133:334053
TITLE: Preparation and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** molecular complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses
INVENTOR(S): Schneck, Jonathan; O'Herrin, Sean; Lebowitz, Michael S.; Hamad, Abdel
PATENT ASSIGNEE(S): The Johns Hopkins University, USA
SOURCE: U.S., 41 pp., Cont.-in-part of U.S. 6,015,884. applicant
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 6140113	A	20001031	US 1998-63276	19980421
US 6015884	A	20000118	US 1997-828712	19970328
US 2002006903	A1	20020117	US 2001-789720	20010222

applicant

PRIORITY APPLN. INFO.:
US 1996-14367 P 19960328
US 1997-828712 A2 19970328
US 1997-58573 P 19970911
US 1998-82538 P 19980421
US 1998-150622 A3 19980910

AB Sol. **multivalent** chimeric TCR/Ig or MHC/Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent immune responses are described. The mol. complexes comprise extracellular domains of **transmembrane heterodimeric** proteins, particularly T cell receptor and major histocompatibility complex proteins, which are covalently linked to the heavy and light chains of Ig mols. to provide sol. **multivalent** mol. complexes with high affinity for their cognate ligands. Studies of the affinity and binding specificity of these **multivalent** chimeric TCR/Ig or MHC/Ig mols. to antigenic peptides are reported. The mol. complexes can be used, inter alia, to detect and regulate antigen-specific T cells and as therapeutic agents for treating disorders involving immune system regulation, such as allergies, autoimmune diseases, tumors, infections, and transplant rejection.

IC ICM C12N015-63
ICS C12N015-09; C12N005-10; C12N015-66; C07H021-00

NCL 435320100

CC 15-3 (Immunochemistry)
Section cross-reference(s): 3, 6, 13

ST TCR receptor **Ig fusion protein** **immune** response modulation; **MHC** class II **Ig** **fusion protein immune** response modulation

IT **Immunoglobulins**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(G1, fusion products, with TCR or **MHC**; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT **Histocompatibility** antigens
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(I-Ek, fusion products, with IgG1; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT **Histocompatibility** antigens
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**MHC** (major **histocompatibility** complex), class II, fusion products, with IgG1; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT **Histocompatibility** antigens
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic

use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**MHC** (major **histocompatibility** complex), class II, .**alpha**., fusion products with IgG1; prepn. and characterization of sol. **multivalent** chimeric **TCR/Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT **Histocompatibility** antigens
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**MHC** (major **histocompatibility** complex), class II, .beta., fusion products with IgG1; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(T-cell-dependent antigens; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT Ligands
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(cognate; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT **Protein** motifs
(extracellular domain; prepn. and characterization of sol. **multivalent chimeric** TCR/**Ig** or **MHC /Ig mol. complexes** to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT **Immunoglobulins**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(heavy chains, fusion products with TCR or **MHC**; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT Autoimmune disease
Disease, animal
Neoplasm
(involving **immune** system, therapy; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT **Immunoglobulins**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(light chains, fusion products with TCR or **MHC**; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT **Immunoglobulins**

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(light chains, .kappa., fusion products with TCR or **MHC**; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT Peptides, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**linker**, between **Ig** light chain and extracellular domain of TCR or **MHC**; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT Infection
(microbial, therapy; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT **Fusion proteins (chimeric proteins)**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(of TCR/**Ig** or **MHC/Ig**; prepn. and characterization of sol. **multivalent chimeric** TCR/**Ig** or **MHC/Ig mol. complexes** to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT **Immunity**
Molecular cloning
Protein engineering
(prepn. and characterization of sol. **multivalent chimeric** TCR/**Ig** or **MHC/Ig mol. complexes** to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT Allergy
Transplant rejection
(therapy; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT **TCR (T cell receptors)**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(.**alpha**., fusion products, with IgG1; prepn. and characterization of sol. **multivalent** chimeric **TCR/Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT TCR (T cell receptors)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(.beta., fusion products, with IgG1; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/**

Ig mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT 127902-44-7 132326-74-0 142606-55-1 152338-19-7 159646-83-0
178561-37-0 181272-91-3 181309-90-0 198695-89-5
RL: PRP (Properties)
(Unclaimed; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT 303983-56-4 303983-57-5
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence of peptide **linker**; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

IT 303815-90-9, 1: PN: US6140113 SEQID: 1 unclaimed DNA 303815-91-0, 2: PN: US6140113 SEQID: 2 unclaimed DNA 303815-92-1, 3: PN: US6140113 SEQID: 3 unclaimed DNA 303815-93-2, 4: PN: US6140113 SEQID: 4 unclaimed DNA 303815-94-3, 5: PN: US6140113 SEQID: 5 unclaimed DNA 303815-95-4, 6: PN: US6140113 SEQID: 6 unclaimed DNA 303815-96-5, 7: PN: US6140113 SEQID: 7 unclaimed DNA 303815-97-6, 8: PN: US6140113 SEQID: 8 unclaimed DNA 303815-98-7, 9: PN: US6140113 SEQID: 9 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; prepn. and characterization of sol. **multivalent** chimeric TCR/**Ig** or **MHC/Ig** mol. complexes to analyze and modulate antigen-specific T cell-dependent **immune** responses)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:573913 HCAPLUS
DOCUMENT NUMBER: 133:149148
TITLE: Protein and cDNA sequences of 5H7 antibody and methods for conferring programmed cell death properties to cells
INVENTOR(S): Woodle, E. Steve; Van, Seventer Jean Maguire; Kulkarni, Sanjay; Kranz, David; Holman, Philmore
PATENT ASSIGNEE(S): Arch Development Corporation, USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047713	A2	20000817	WO 2000-US3234	20000208
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000029858	A5	20000829	AU 2000-29858	20000208

PRIORITY APPLN. INFO.: US 1999-119238 P 19990209

WO 2000-US3234 W 20000208

AB The present invention relates to isolated and purified polynucleotides encoding for the light and heavy variable regions of a 5H7 antibody and methods for using these genes to confer programmed cell death properties to a cell.

IC ICM C12N

CC 15-3 (Immunochemistry)
Section cross-reference(s): 3

ST cDNA sequences 5H7 antibody **chimeric protein** apoptosis

IT **Fusion proteins** (**chimeric proteins**)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(5H7 light variable region/**linker1**/5H7 heavy variable region/**linker2**; **protein** and cDNA sequences of 5H7 antibody and methods for conferring programmed cell death properties to cells)

IT **Chimeric** gene
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(5H7 light variable region/**linker1**/5H7 heavy variable region/**linker2**; **protein** and cDNA sequences of 5H7 antibody and methods for conferring programmed cell death properties to cells)

IT **Histocompatibility** antigens
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(HLA-A2, binding with 5H7 antibody; protein and cDNA sequences of 5H7 antibody and methods for conferring programmed cell death properties to cells)

IT **Histocompatibility** antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**MHC** (major **histocompatibility** complex), class I, 5H7 antibody against; protein and cDNA sequences of 5H7 antibody and methods for conferring programmed cell death properties to cells)

IT 142244-28-8, DNA (mouse clone pMc5-Kb MA-15C5 **immunoglobulin** G .kappa.-chain precursor signal peptide-specifying)
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; protein and cDNA sequences of 5H7 antibody and methods for conferring programmed cell death properties to cells)

L34 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:278008 HCAPLUS
DOCUMENT NUMBER: 132:320955
TITLE: Interferon-beta **fusion proteins** and uses
INVENTOR(S): Whitty, Adrian; Runkel, Laura; Brickelmaier, Margot; Hochman, Paula
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000023472	A2	20000427	WO 1999-US24200	19991015
WO 2000023472	A3	20000831		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1121382	A2	20010808	EP 1999-956574	19991015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9915548	A	20010814	BR 1999-15548	19991015
NO 2001001861	A	20010613	NO 2001-1861	20010411

PRIORITY APPLN. INFO.:

US 1998-104491	P	19981016
US 1999-120237	P	19990216
WO 1999-US24200	W	19991015

AB A fusion polypeptide is described having the amino acid sequence X-Y-Z, or portion thereof, comprising the amino acid sequence of a glycosylated interferon-.beta. (X); Y is an optional linker moiety; and Z is a polypeptide comprising at least a portion of a polypeptide other than glycosylated interferon-.beta.. It is preferred that X is a human interferon-.beta.-1a, and Z is the const. region of an Ig of the class selected from IgM, IgG, IgD, IgA, and IgE. Mutants of interferon-.beta.-1a are also described. The fusion proteins are capable of inhibiting angiogenesis or neovascularization and are useful for treating multiple sclerosis, fibrosis, inflammatory or autoimmune diseases, cancers, hepatitis and other viral diseases.

IC ICM C07K014-565
ICS C12N015-62; C07K019-00
CC 15-5 (Immunochemistry)
Section cross-reference(s): 3
ST interferon beta **Ig fusion protein**
antiangiogenic

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(A; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT Lymphoma
(Burkitt's, Daudi cell line; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(D; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT Animal cell line
(Daudi; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(E; interferon-.beta.-**Ig. fusion proteins**
for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G1; interferon-.beta.-**Ig. fusion proteins**
for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G2; interferon-.beta.-**Ig. fusion proteins**
for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G2a; interferon-.beta.-**Ig. fusion proteins**
for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G3; interferon-.beta.-**Ig. fusion proteins**
for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G4; interferon-.beta.-**Ig. fusion proteins**
for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G; interferon-.beta.-**Ig. fusion proteins**
for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M; interferon-.beta.-**Ig. fusion proteins**
for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT **Histocompatibility** antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**MHC** (major **histocompatibility** complex), class I; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT **Histocompatibility** antigens

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**MHC** (major **histocompatibility** complex), class II; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(for interferon .beta.; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**fusion protein**; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heavy chains, **fusion protein**; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT Angiogenesis
Angiogenesis inhibitors
Antiviral agents
Autoimmune disease
Cytolysis
DNA sequences
Fibrosis
Hepatitis
Inflammation
Molecular cloning
Multiple sclerosis
Neoplasm
Proliferation inhibition
Protein sequences
(interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT **Fusion proteins** (**chimeric proteins**)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT Interferon receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT CD1 (antigen)
CD2 (antigen)
CD4 (antigen)
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(interferon-.beta.-**Ig. fusion proteins**
for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT Polymers, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(interferon-.beta.-**Ig. fusion proteins**
for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT Polyoxyalkylenes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(interferon-.beta.-**Ig. fusion proteins**
for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT Angiogenesis
(neovascularization; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT Infection
(viral; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT Interferons
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(.beta., 1a; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT Interferons
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(.beta.; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT 266300-49-6 266331-72-0 266331-74-2 266331-76-4
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT 9014-74-8, Enterokinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**linker** sequence; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT 266300-48-5 266331-71-9 266331-73-1 266331-75-3
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; interferon-.beta.-**Ig. fusion proteins** for use as angiogenesis inhibition and for treating inflammation, autoimmune disease and cancer)

IT 266299-87-0, 5: PN: WO0023472 PAGE: 33 unclaimed DNA 266299-88-1, 7: PN: WO0023472 PAGE: 33 unclaimed DNA 266299-89-2, 8: PN: WO0023472 PAGE: 33 unclaimed DNA 266299-90-5, 9: PN: WO0023472 PAGE: 33 unclaimed DNA 266299-91-6, 10: PN: WO0023472 TABLE: 2 unclaimed DNA 266299-92-7, 11: PN: WO0023472 TABLE: 2 unclaimed DNA 266299-93-8, 12: PN: WO0023472 TABLE: 2 unclaimed DNA 266299-94-9, 13: PN: WO0023472 TABLE: 2 unclaimed

DNA 266299-95-0, 14: PN: WO0023472 TABLE: 2 unclaimed DNA 266299-96-1, 15: PN: WO0023472 TABLE: 2 unclaimed DNA 266299-97-2, 16: PN: WO0023472 TABLE: 2 unclaimed DNA 266299-98-3, 17: PN: WO0023472 TABLE: 2 unclaimed DNA 266299-99-4, 18: PN: WO0023472 TABLE: 2 unclaimed DNA 266300-00-9, 19: PN: WO0023472 TABLE: 2 unclaimed DNA 266300-01-0, 20: PN: WO0023472 TABLE: 2 unclaimed DNA 266300-02-1, 21: PN: WO0023472 TABLE: 2 unclaimed DNA 266300-03-2, 22: PN: WO0023472 TABLE: 2 unclaimed DNA 266300-04-3, 23: PN: WO0023472 TABLE: 2 unclaimed DNA 266300-05-4, 24: PN: WO0023472 TABLE: 2 unclaimed DNA 266300-06-5, 25: PN: WO0023472 TABLE: 2 unclaimed DNA 266300-07-6, 26: PN: WO0023472 TABLE: 2 unclaimed DNA 266300-08-7, 27: PN: WO0023472 TABLE: 2 unclaimed DNA 266300-09-8, 28: PN: WO0023472 PAGE: 47 unclaimed DNA 266300-10-1, 29: PN: WO0023472 PAGE: 47 unclaimed DNA 266300-11-2, 30: PN: WO0023472 PAGE: 47 unclaimed DNA 266300-12-3, 31: PN: WO0023472 PAGE: 47 unclaimed DNA 266300-13-4, 32: PN: WO0023472 PAGE: 48 unclaimed DNA 266300-14-5, 33: PN: WO0023472 PAGE: 48 unclaimed DNA 266300-15-6, 34: PN: WO0023472 PAGE: 51 unclaimed DNA 266300-16-7, 35: PN: WO0023472 PAGE: 51 unclaimed DNA 266300-17-8, 37: PN: WO0023472 PAGE: 51 unclaimed DNA

RL: PRP (Properties)
(unclaimed nucleotide sequence; interferon-beta **fusion proteins** and uses)

IT 266300-18-9 266300-19-0 266300-20-3 266300-21-4 266300-22-5 266300-23-6

RL: PRP (Properties)
(unclaimed sequence; interferon-beta **fusion proteins** and uses)

L34 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:277860 HCAPLUS
DOCUMENT NUMBER: 132:320940
TITLE: Polyspecific binding molecules and uses thereof
INVENTOR(S): Weidanz, Jon A.; Card, Kimberlyn; Sherman, Linda A.; Klinman, Norman R.; Wong, Hing C.
PATENT ASSIGNEE(S): Sunol Molecular Corporation, USA
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000023087	A1	20000427	WO 1999-US24645	19991021
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1124568	A1	20010822	EP 1999-970601	19991021
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-105164 P 19981021
WO 1999-US24645 W 19991021

AB The present invention relates to polyspecific binding mols. and particularly single-chain polyspecific binding mols. that include at least

one single-chain T-cell receptor (s.c.-TCR) covalently linked through a peptide linker sequence to at least one single-chain antibody (s.c.-Ab). The polyspecific binding mols. activate immune cells (e.g. cytotoxic T cells, NK cells or macrophages) and kill target cells (e.g. tumor cells or virally infected cells). The polyspecific binding mols. are useful for diagnosis and treatment of cancers and viral infections.

IC ICM A61K035-26
ICS A61K039-395; C07K016-00

CC 15-3 (Immunochemistry)
Section cross-reference(s): 3

ST TCR **Ig** single chain **fusion protein**; tumor viral infection **chimeric** TCR **Ig**

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G, TCR **fusion protein**; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT **Histocompatibility** antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA-A2; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT **Histocompatibility** antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT **Histocompatibility** antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**MHC** (major **histocompatibility** complex); polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Biomarkers (biological responses)
(activation mol.; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Diagnosis
(agents; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-erbB2, protein product; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Diagnosis
(cancer; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT T cell (lymphocyte)
(cytotoxic; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Neoplasm
(diagnosis; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragments; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(heavy chains; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Genetic element
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(leader sequence; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(light chains; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Peptides, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**linker**; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Lymphocyte
(natural killer cell; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT **Proteins**, specific or class
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pVIII, TCR **fusion protein**; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Gene, microbial
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pelB; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Gene, microbial
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phoA; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Antitumor agents
Culture media
Cytomegalovirus
Escherichia coli
Genetic vectors
Hybridoma
Imaging agents
Labels
Lymphocyte
Macrophage
Molecular cloning
Neoplasm
Protein sequences
T cell (lymphocyte)
Test kits
(polyspecific binding mols. comprising single chain TCR and **Ig**

for diagnosis and therapy of tumor or viral infection)

IT Enhancer (genetic element)
Polynucleotides
Promoter (genetic element)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT **Fusion proteins (chimeric proteins)**
TCR (T cell receptors)
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Antigens
CD28 (antigen)
CD3 (antigen)
p53 (protein)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Antibodies
Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Genetic element
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(signal sequence; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Proteins, general, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tag; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT Infection
(viral; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT 122024-47-9P 149298-29-3P 265653-00-7P 265653-01-8P
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptide **linker**; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT 265653-03-0P 265653-04-1P
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT 157048-07-2
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)

IT 82123-81-7P 265653-02-9P 265992-78-7P

RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein tag; polyspecific binding mols. comprising single chain TCR and **Ig** for diagnosis and therapy of tumor or viral infection)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:795994 HCAPLUS
DOCUMENT NUMBER: 132:31744
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Ltd., UK
SOURCE: PCT Int. Appl., 745 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964627	A2	19991216	WO 1999-GB1780	19990604

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

GB 1998-12099	A	19980606
GB 1998-13291	A	19980620
GB 1998-13611	A	19980624
GB 1998-13835	A	19980627
GB 1998-14110	A	19980701
GB 1998-14580	A	19980707
GB 1998-15438	A	19980716
GB 1998-15574	A	19980718
GB 1998-15576	A	19980718
GB 1998-16085	A	19980724
GB 1998-16086	A	19980724
GB 1998-16921	A	19980805
GB 1998-17097	A	19980807
GB 1998-17200	A	19980808
GB 1998-17632	A	19980814
GB 1998-17943	A	19980819

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and

their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic.RTM." profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

IC ICM C12Q001-68
ICS C07K016-18

CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 9, 13, 14

IT Chromogranins
Cyclins
Glycophorins
Immunoglobulins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(A, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Apolipoproteins**
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(A-I, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Apolipoproteins
Cyclins
Immunoglobulins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(D, core group of **disease**-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Apolipoproteins
Cadherins
Immunoglobulins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(E, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Immunoglobulins**
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(G2, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Histocompatibility** antigens
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(HLA-DP, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Histocompatibility** antigens
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL

(Biological study); USES (Uses)
(HLA-DQ, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Histocompatibility** antigens
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(HLA-DR, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Immunoglobulin** receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(IgE type II, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Immunoglobulin** receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(IgG type I, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Immunoglobulin** receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(IgG type IIA, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Immunoglobulins**
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(J protein, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Immunoglobulins**
Laminins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(M, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Histocompatibility** antigens
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**MHC** (major **histocompatibility** complex), class I, A and B and C, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Histocompatibility** antigens
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**MHC** (major **histocompatibility** complex), class II, complementation group A and B and C and D, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT ACTH receptors
Albumins, biological studies
Amelogenins
Amyloid precursor proteins
Androgen receptors
Aromatic hydrocarbon receptors
Arrestins
Benzodiazepine receptors
CD1 (antigen)
CD14 (antigen)
CD19 (antigen)
CD2 (antigen)
CD20 (antigen)

CD22 (antigen)
CD26 (antigen)
CD28 (antigen)
CD3 (antigen)
CD34 (antigen)
CD36 (antigen)
CD38 (antigen)
CD4 (antigen)
CD40 (antigen)
CD44 (antigen)
CD45 (antigen)
CD5 (antigen)
CD59 (antigen)
CD68 (antigen)
CD69 (antigen)
CD7 (antigen)
CD8 (antigen)
CD80 (antigen)
CD86 (antigen)
CFTR (cystic fibrosis **transmembrane** conductance regulator)
CTLA-4 (antigen)
Calcitonin gene-related peptide receptors
Calcitonin receptors
Calnexin
Calretinin
Cannabinoid receptors
Carcinoembryonic antigen
Cell adhesion molecules
Ciliary neurotrophic factor
Clathrin
Clusterin
Corticosteroid receptors
Corticotropin releasing factor receptors
Cyclophilins
Desmins
Dynamin
Dyneins
Dystrophin
Elastins
Epidermal growth factor receptors
Erythropoietin receptors
FSH receptors
Fas antigen
Ferritins
Fibrinogens
Fibronectins
GTPase-activating protein
Gastrin-releasing peptide receptors
Gelsolin
Glucagon receptors
Glucagon-like peptide-1 receptors
Glucocorticoid receptors
Gonadotropin receptors
Gonadotropin-releasing hormone receptor
Growth factor receptors
Growth hormone receptors
Growth hormone-releasing hormone receptors
Hemoglobins
Hemopexins
Hepatocyte growth factor

Heregulins
Immunoglobulin receptors
Insulin receptors
Insulin-like growth factor I receptors
Insulin-like growth factor II receptors
Interleukin 1 receptor antagonist
Interleukin 1 receptors
Interleukin 10
Interleukin 11
Interleukin 13
Interleukin 1.alpha.
Interleukin 1.beta.
Interleukin 3
Interleukin 3 receptors
Interleukin 4
Interleukin 4 receptors
Interleukin 5
Interleukin 5 receptors
Interleukin 6
Interleukin 6 receptors
Interleukin 7
Interleukin 7 receptors
Interleukin 8
Interleukin 8 receptors
Interleukin 9
Intrinsic factors
Invariant chain (class II antigen)
LFA-3 (antigen)
Lactoferrins
Leptin receptors
Leukemia inhibitory factor
Leukemia inhibitory factor receptors
Leukosialin
Lymphotoxin
Macrophage colony-stimulating factor receptors
Macrophage inflammatory protein 2
Metallothioneins
Mineralocorticoid receptors
Moesins
Monocyte chemoattractant protein-1
Multidrug resistance proteins
Myelin P0 protein
Myelin basic protein
Myoglobins
Nerve growth factor receptors
Neurotensin receptors
Nicotinic receptors
Opioid receptors
Osteocalcins
Osteonectin
Osteopontin
Oxytocin receptors
Parathyroid hormone receptors
Parvalbumins
Pituitary adenylate cyclase-activating polypeptide receptor
Platelet-activating factor receptors
Platelet-derived growth factor receptors
Platelet-derived growth factors
Prion proteins
Progesterone receptors

Prolactin receptors
Proliferating cell nuclear antigen
Prostanoid receptors
Proteolipid protein
Radixin
Ras proteins
Rhodopsins
Ryanodine receptors
Secretin receptors
Stem cell factor
Sulfonylurea receptors
Synaptophysin
TCR .alpha..beta. (receptor)
Talin
Tau factor
Tenascins
Thrombin receptors
Thrombomodulin
Thrombospondins
Thromboxane receptors
Thyroglobulin
Thyrotropin receptors
Thyrotropin-releasing hormone receptors
Titins
Transcortins
Transferrin receptors
Transferrins
Transthyretin
Tubulins
Tumor necrosis factor receptors
Tumor necrosis factors
Urokinase-type plasminogen activator receptors
VIP receptors
Vasopressin receptors
Villin
Vimentins
Vinculin
Vitamin D receptors
neu (receptor)
p53 (protein)
.alpha.-Fetoproteins
.alpha.1-Acid glycoprotein
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Behavior
Development, mammalian postnatal
Immunity
Metabolism, animal
Sexual behavior
(disorder, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

L34 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:686556 HCAPLUS
DOCUMENT NUMBER: 131:321529
TITLE: Vaccines for treatment of lymphoma and leukemia
INVENTOR(S): Denney, Dan W., Jr.
PATENT ASSIGNEE(S): Genitope Corporation, USA

SOURCE: U.S., 90 pp., Cont.-in-part of U.S. 5,776,746.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5972334	A	19991026	US 1996-761277	19961206
US 5776746	A	19980707	US 1996-644664	19960501
CA 2248653	AA	19971106	CA 1997-2248653	19970425
WO 9741244	A1	19971106	WO 1997-US7039	19970425
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9728145	A1	19971119	AU 1997-28145	19970425
AU 716257	B2	20000224		
EP 910655	A1	19990428	EP 1997-922496	19970425
R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
NO 9805068	A	19981228	NO 1998-5068	19981030

PRIORITY APPLN. INFO.: US 1996-644664 19960501
US 1996-761277 19961206
WO 1997-US7039 19970425

AB The present invention provides **multivalent** vaccines for the treatment of B-cell malignancies (e.g., lymphomas and leukemias). The present invention also provides methods for the prodn. of custom vaccines, including **multivalent** vaccines for the treatment of immune cell tumors malignancies as well as methods of treating immune cell tumors using custom vaccines. The vaccines are expressed by transformed T lymphoid cells comprising amplification vector encoding inhibitable enzyme and expression vector encoding Ig. VH (VL) of B lymphoma or its fusion protein with an immune-enhancing cytokine. The inhibitable enzyme is selected from dihydrofolate reductase, glutamine synthetase, adenosine deaminase and asparagine synthetase.

IC ICM A61K329-395
ICS C12P021-08; C12N015-13; C12N005-10
NCL 424131100
CC 15-2 (Immunochemistry)
Section cross-reference(s): 3
ST vaccine B T cell lymphoma leukemia; inhibitable enzyme **Ig** heavy light chain variable

IT **Histocompatibility** antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**MHC** (major **histocompatibility** antigen complex), class II; vaccines for treatment of lymphoma and leukemia)

IT Cytokines
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chimeric **Ig**. VH or VL; vaccines for treatment of lymphoma and leukemia)

IT **Immunoglobulins**

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heavy chains, variable; vaccines for treatment of lymphoma and leukemia)

IT Leukemia
Lymphoma
(**immune** cell; vaccines for treatment of lymphoma and leukemia)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(light chains, variable; vaccines for treatment of lymphoma and leukemia)

IT **Fusion proteins** (**chimeric proteins**)
Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(vaccines for treatment of lymphoma and leukemia)

IT 76560-38-8, **Immunoglobulin** (human Inv3 allele C.kappa. protein moiety reduced) 82030-18-0, **Immunoglobulin** G (human C.gamma.4 protein moiety reduced) 84136-33-4 158572-06-6 248921-42-8 248921-48-4 248921-73-5 249301-92-6
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; vaccines for treatment of lymphoma and leukemia)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:549393 HCAPLUS
DOCUMENT NUMBER: 131:183867
TITLE: Monovalent, **multivalent**, and multimeric **MHC** binding domain **fusion proteins** and conjugates, and uses therefor
INVENTOR(S): Wucherpfennig, Kai W.; Strominger, Jack L.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9942597	A1	19990826	WO 1999-US3603	19990219
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9927748	A1	19990906	AU 1999-27748	19990219
BR 9908082	A	20001031	BR 1999-8082	19990219

EP 1054984 A1 20001129 EP 1999-908272 19990219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRIORITY APPLN. INFO.: US 1998-75351 P 19980219
WO 1999-US3603 W 19990219

AB The present invention is directed to the design, prodn., and use of monovalent, **multivalent** and multimeric major histocompatibility complex binding domain fusion proteins and conjugates. The MHC fusion proteins and conjugates may comprise MHC class II .alpha. or .beta. chain (HLA-DRA*0101, HLA-DRA*0102, HLA-DQA1*0301, HLA-DRB1*01, etc.), leucine zipper domain of Fos or Jun, linker peptide, yeast .sigma.-mating factor secretion signal, human myelin basic protein tag, IgG or IgE or IgM Fc, and optionally cytotoxic substance (human desmoglein 3 protein peptide). The MHC binding domain fusion proteins and conjugates are useful for diagnosis and treatment of diseases assocd. with T cell-mediated immune response and antigen presentation, e.g. autoimmune disease, multiple sclerosis and rheumatoid arthritis. Thus, fusion proteins contg. HLA-DR2 .alpha. chain (.beta. chain), Fos (Jun) leucine zipper dimerization domain, VDGGGGG linker, and .alpha.-mating secretion signal were prepd., fused with IgG2a or IgM, tagged with MBP peptide, conjugated with bead carrier, and used for selectively depletion of T cells.

IC ICM C12N015-62
ICS C07K019-00; C07K017-00; G01N033-53; A61K035-14; A61K047-48; C07K014-705; C07K016-00

CC 15-2 (Immunochemistry)
Section cross-reference(s): 3

ST **MHC fusion protein** conjugate autoimmune disease; **Ig** HLA Fos Jun T cell

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A, **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Leukemia
(B-cell; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(D, **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E, **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G, **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated

immune response and antigen presentation)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G2a, **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT **Histocompatibility** antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DQ1, **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT **Histocompatibility** antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DQ2, **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT **Histocompatibility** antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DQ8, **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DQA1*0301 **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DQA1*0501 **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DQB1*02 **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(HLA-DQB1*03 **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DQB5*01 **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT **Histocompatibility** antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DR1, **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT **Histocompatibility** antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DR2, **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT **Histocompatibility** antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DR4, **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DRA*0101 **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DRA*0102 **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DRB1*01 **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DRB1*15 **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DRB1*16 **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Gene, animal
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Jun, **proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(M, **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT **Histocompatibility** antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**MHC** (major **histocompatibility** antigen complex), class II, **fusion proteins**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT **Immunity**
(T cell-mediated; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Spheres
(bead; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Polymers, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(branched; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Polymers, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-; multimeric **MHC** binding domain **fusion**

proteins and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Toxins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(desmoglein III; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Carboxylic acids, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dicarboxylic, polyanhydrides; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Transcription factors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fos; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragments, const. region; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heavy chains; const. region; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Carboxylic acids, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxy, polyesters; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT **Protein** motifs
(leucine zipper; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)
IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(light chains, const. region; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)
IT Gangliosides
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monosialogangliosides; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)
IT Adoptive immunotherapy
Antigen presentation
Antigen-presenting cell
Apoptosis
Autoimmune disease
Biodegradable materials
Carriers
Cytotoxic agents
DNA sequences
Disulfide group
Fluorescent substances
Immune tolerance
Liposomes
Multiple sclerosis
Particles
Protein sequences
Rheumatoid arthritis
T cell (lymphocyte)
Yeast
(multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)
IT **Fusion proteins** (**chimeric proteins**
)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)
IT CD19 (antigen)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)
IT Dendritic polymers
Glass, biological studies
Nucleic acids

Phosphatidic acids
Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Phosphatidylglycerols
Phosphatidylinositols
Phosphatidylserines
Polyanhydrides
Polyethers, biological studies
Polyoxyalkylenes, biological studies
Polythioethers
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multimeric **MHC** binding domain **fusion** **proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Polyamides, biological studies
Polysiloxanes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multimeric **MHC** binding domain **fusion** **proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Molecules
(neg. charged; multimeric **MHC** binding domain **fusion** **proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Lecithins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovo-; multimeric **MHC** binding domain **fusion** **proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Myelin basic **protein**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide tag; multimeric **MHC** binding domain **fusion** **proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Polyamines
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyalkylene-; multimeric **MHC** binding domain **fusion** **proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Alcohols, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyamido-; multimeric **MHC** binding domain **fusion** **proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Amines, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyamines, nonpolymeric, amido; multimeric **MHC** binding

domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Polymers, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyaryl; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Coiled-coil
(**protein**; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT .alpha.-Factor (microbial)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(secretion signal sequence; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT Genetic element
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(signal sequence, secretory; multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT 446-72-0, Genistein
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT 203592-09-0 203592-10-3 203592-11-4 203592-12-5 203592-13-6 203592-14-7 240412-51-5 240412-52-6
RL: PRP (Properties)
(multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

IT 57-88-5, Cholesterol, biological studies 58-85-5, Biotin 124-30-1, Stearyl amine 2197-63-9, Dicetyl phosphate 7631-86-9, Silica, biological studies 25322-68-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multimeric **MHC** binding domain **fusion proteins** and conjugates for diagnosis and treatment of diseases assocd. with T cell-mediated **immune** response and antigen presentation)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:194281 HCAPLUS
DOCUMENT NUMBER: 130:236471
TITLE: Use of **multivalent** chimeric peptide-loaded, **MHC/Ig** molecules to detect, activate or suppress antigen-specific T cell-dependent **immune** responses

INVENTOR(S): Schneck, Jonathan; Pardoll, Drew; O'herrin, Sean M.; Slansky, Jill; Greten, Tim
PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine, USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9913095	A2	19990318	WO 1998-US18909	19980911
WO 9913095	A3	19990610		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6268411	B1	20010731	US 1998-150622	19980910
AU 9894776	A1	19990329	AU 1998-94776	19980911
EP 1012320	A2	20000628	EP 1998-948143	19980911
R: AT, BE, DE, DK, ES, FR, GB, IT, NL, SE, IE				
JP 2001515726	T2	20010925	JP 2000-510880	19980911
US 2002006903	A1	20020117	US 2001-789720	20010222

PRIORITY APPLN. INFO.:

US 1997-58573	P	19970911
US 1998-82538	P	19980421
US 1997-828712	A2	19970328
US 1998-150622	A3	19980910
WO 1998-US18909	W	19980911

AB To increase the effective affinity of sol. analogs of peptide/MHC mols. for their cognate ligands, divalent peptide/MHC complexes were constructed. Using a recombinant DNA strategy, DNA encoding the MHC class I was ligated to DNA coding for murine Ig heavy chain. MHC/Ig complexes were exploited to homogeneously load with peptides of interest. The results of flow cytometry demonstrated that the pepMHC/Ig complexes bound specifically with high affinity to cells bearing their cognate receptors. pepMHC/Ig complexes are also useful in modulating effector functions of antigen-specific T cells. These pepMHC/Ig complexes are useful for studying TCR/MHC interactions and lymphocyte tracking and have uses as specific regulators of immune responses. The MHC/Ig complexes are also useful for treating allergy, organ transplant, autoimmune disease, tumor and infectious disease.

IC ICM C12N015-85
ICS A61K038-17; A61K039-395; A61K047-48; A61K039-21; A61K039-145; A61K035-12; G01N033-53; A61K039-395; A61K039-145; A61K038-17; A61K039-395; A61K039-21; A61K038-18

CC 15-3 (Immunochemistry)
Section cross-reference(s): 3

ST **MHC Ig** chimeric peptide **immunomodulator**; antigen specific T cell **immune** response

IT Endotoxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Pseudomonas; use of **multivalent** chimeric peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

IT Pseudomonas

(endotoxin; use of **multivalent** chimeric peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

IT Parasite
(infection; use of **multivalent** chimeric peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

IT **Proteins** (specific **proteins** and subclasses)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(influenza AM; use of **multivalent chimeric** peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

IT gag **proteins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p17gag; use of **multivalent chimeric** peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

IT Allergies
Autoimmune diseases
Bacterial infection
Bone marrow diseases
CD8-positive T cell
Cerebrospinal fluid
Cytotoxic T cell
Dendritic cell
Flow cytometry
Genetic vectors
Human T-lymphotropic virus
Human T-lymphotropic virus 1
Human immunodeficiency virus
Immunotherapy
Infection
Molecular cloning
Mycosis
Pathogen
Protein sequences
T cell (lymphocyte)
Transplant (organ)
Tropical spastic paraparesis
Tumors (animal)
Vaccines
Viral infection
(use of **multivalent chimeric** peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

IT Inflammatory cytokines
Interferon .gamma.
Lymphokines
Tumor necrosis factor .alpha.
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(use of **multivalent** chimeric peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

IT Class I **MHC** antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(use of **multivalent** chimeric peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

IT Class II **MHC** antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of **multivalent** chimeric peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

IT **Fusion proteins** (**chimeric proteins**)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of **multivalent chimeric** peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of **multivalent** chimeric peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

IT **MHC** antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of **multivalent** chimeric peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

IT Alloantigens
Antigens
Genes (animal)
IgG
IgG1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(use of **multivalent** chimeric peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

IT CD4 (antigen)
HLA-DR antigen
Tax **protein**
Tumor-associated antigen
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of **multivalent chimeric** peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

IT Class I HLA antigens
HLA-A2 antigen
Immunoglobulin heavy chains
Ricins
Toxins
.beta.2-Microglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of **multivalent** chimeric peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

IT 141368-69-6 141677-18-1 147468-65-3
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of **multivalent** chimeric peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)
IT 9031-11-2, .beta.-Galactosidase
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of **multivalent** chimeric peptide-loaded **MHC/Ig** mols. to detect, activate or suppress antigen-specific T cell-dependent **immune** responses)

L34 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:191154 HCAPLUS
DOCUMENT NUMBER: 131:57491
TITLE: Soluble, high-affinity dimers of T-cell receptors and class II major **histocompatibility** complexes: Biochemical probes for analysis and modulation of **immune** responses
AUTHOR(S): Lebowitz, Michael S.; O'Herrin, Sean M.; Hamad, Abdel-Rahim A.; Fahmy, Tarek; Marguet, Didier; Barnes, Nicholas C.; Pardoll, Drew; Bieler, Joan G.; Schneck, Jonathan P.
CORPORATE SOURCE: Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD, USA
SOURCE: Cell. Immunol. (1999), 192(2), 175-184
CODEN: CLIMB8; ISSN: 0008-8749
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB T cell receptors (TCR) and major histocompatibility complex (MHC) mols. are integral membrane proteins that have central roles in cell-mediated immune recognition. Therefore, sol. analogs of these mols. would be useful for analyzing and possibly modulating antigen-specific immune responses. However, due to the intrinsic low-affinity and inherent soly. problems, it has been difficult to produce sol. high-affinity analogs of TCR and class II MHC mols. This report describes a general approach which solves this intrinsic low-affinity by constructing sol. divalent analogs using IgG as a mol. scaffold. The divalent nature of the complexes increases the avidity of the chimeric mols. for cognate ligands. The generality of this approach was studied by making sol. divalent analogs of two different classes of proteins, a TCR (2C TCR2Ig) and a class II MHC (MCCI-Ek2Ig) mol. Direct flow cytometry assays demonstrate that the divalent 2C TCR2Ig chimera retained the specificity of the native 2C TCR, while displaying increased avidity for cognate peptide/MHC ligands, resulting in a high-affinity probe capable of detecting interactions that heretofore have only been detected using surface plasmon resonance. TCR2IgG was also used in immunofluorescence studies to show ER localization of intracellular peptide-MHC complexes after peptide feeding. MCCI-Ek2Ig chimeras were able to both stain and activate an MCC-specific T cell hybridoma. Construction and expression of these two diverse **heterodimers** demonstrate the generality of this approach. Furthermore, the increased avidity of these sol. divalent proteins makes these chimeric mols. potentially useful in clin. settings for probing and modulating in vivo cellular responses. (c) 1999 Academic Press.
CC 15-2 (Immunochemistry)
ST TCR receptor **Ig fusion protein; MHC** class II **Ig fusion protein**
IT **Immunoglobulins**

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(Gl, fusion products, with TCR receptors or **MHC** class II; prepn. and biol. activity of sol. high-affinity dimers of T-cell receptors and class II **MHC**)

IT **Histocompatibility** antigens
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(I-Ek, fusion products, with IgG1; prepn. and biol. activity of sol. high-affinity dimers of T-cell receptors and class II **MHC**)

IT **Histocompatibility** antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**MHC** (major **histocompatibility** antigen complex), class II, complexes, with peptides; sol. high-affinity dimers of T-cell receptors bind to)

IT Peptides, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(complexes, with **MHC** class II; sol. high-affinity dimers of T-cell receptors bind to)

IT **TCR .alpha..**beta. (receptor)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(fusion products, with IgG1; prepn. and biol. activity of sol. high-affinity dimers of **T-cell receptors** and class II **MHC**)

IT **Fusion proteins** (**chimeric proteins**)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and biol. activity of sol. high-affinity dimers of T-cell receptors and class II **MHC**)

IT Endoplasmic reticulum
(sol. high-affinity dimers of T-cell receptors bind to **MHC** class II/peptide complexes in)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:96139 HCAPLUS
DOCUMENT NUMBER: 130:167161
TITLE: Directed cytolysis of target cells, agents and compositions causing cytolysis, and compounds that can be used to produce the agents
INVENTOR(S): Soegaard, Morten; Abrahmsen, Lars; Lando, Peter; Forsberg, Goran; Kalland, Terje; Dohlsten, Mikael
PATENT ASSIGNEE(S): Pharmacia & Upjohn Ab, Swed.
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9904820	A2	19990204	WO 1998-EP4219	19980702
WO 9904820	A3	19990812		

W: AU, BG, BR, CA, CN, CZ, HU, ID, IL, JP, KR, MX, NO, NZ, PL, RO, SG, SI, UA, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE

AU 9884415	A1	19990216	AU 1998-84415	19980702
EP 998305	A2	20000510	EP 1998-935025	19980702
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
BR 9815493	A	20001031	BR 1998-15493	19980702
JP 2001510687	T2	20010807	JP 2000-503871	19980702
ZA 9806431	A	19990127	ZA 1998-6431	19980720
NO 2000000265	A	20000315	NO 2000-265	20000119

PRIORITY APPLN. INFO.: US 1997-53211 P 19970721
SE 1997-4170 A 19971114
WO 1998-EP4219 W 19980702

AB A method for inactivating target cells in the presence of T cells by bringing the two types of cells in contact with a superantigen (SAg) in the presence of an immune modulator, characterized in that at least one of the superantigen and the immune modulator is in the form of a conjugate between a "free" superantigen (SAg) and a moiety targeting the conjugate to the target cells. A superantigen conjugate complying with the formula (I): (T)x(SAg)y(IM)z; (a) T is a targeting moiety, SAg corresponds to a free superantigen, IM is an immune modulator that is not a superantigen and T, SAg and IM are linked together via org. linkers B; (b) x, y and z are integers that typically are selected among 0-10 and represent the no. of moieties T, SAg and IM, resp., in a given conjugate mol., with the provision that y > 0 and also one or both of x and z > 0. The superantigen conjugate is preferably a triple fusion protein. A targeted immune modulator, characterized in that it is a conjugate between a targeting moiety (T''') and a modified immune modulator (IM'''). The conjugate complies with a formula analogous to formula (I) except for the imperative presence of the modified immune modulator. A superantigen moiety may be present. A DNA mol. encoding a superantigen and an immune modulator. Thus, triple fusion proteins contg. CD80 or interleukin 2, anti-C215 antigen Fab, and Staphylococcal enterotoxin A were prepd. and used for tumor therapy.

IC ICM A61K047-48

CC 15-2 (Immunochemistry)
Section cross-reference(s): 1, 63

ST superantigen cytokine antibody receptor **fusion protein** ; tumor therapy **immunomodulator** superantigen targeting moiety

IT **Immunoglobulin** light chains
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C215 antibody; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C215; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT Anergy
(T cell; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT **Immunomodulators**
(conjugates; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT Cytokine receptors
Immunoglobulins

Interleukin 2
Staphylococcal enterotoxin A
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT CD80 (antigen)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT CD86 (antigen)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT Superantigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT Chemokines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT Animal cells
(diseased cell targeting and inactivation; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT Antitumor agents
(**fusion proteins**; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT Oligopeptides
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**linker**; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT Ligands
Receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lymphocyte surface; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT Diseases (animal)
(target cell-assocd.; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT Leukemia

Lymphoma
(targetting therapy; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT Cytolysis
Tumors (animal)
(targetting; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT Lymphocyte
Mutation
Protein sequences
Serum (blood)
Signal transduction (biological)
T cell (lymphocyte)
T cell activation
(triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT Antibody conjugates
Fusion proteins (**chimeric proteins**)
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT Class II **MHC** antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT CD28 (antigen)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT DNA
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

IT 14379-76-1 220365-25-3 220365-26-4 220365-27-5 220365-28-6 220365-29-7
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates contg.; triple conjugate or **fusion protein** contg. targeting moiety and superantigen and **immunomodulator** mol. for targeting cytolysis and for tumor therapy)

L34 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:542979 HCAPLUS
DOCUMENT NUMBER: 129:174681
TITLE: Soluble CTLA4 mutant molecules and uses thereof
INVENTOR(S): Peach, Robert James; Naemura, Joseph Roy; Linsley,

Peter S.; Bajorath, Jurgen
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9833513	A1	19980806	WO 1998-US1880	19980129
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9860525	A1	19980825	AU 1998-60525	19980129
AU 725016	B2	20001005		
BR 9806764	A	20000314	BR 1998-6764	19980129
EP 988047	A1	20000329	EP 1998-903873	19980129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001510473	T2	20010731	JP 1998-533143	19980129
NO 9903708	A	19990928	NO 1999-3708	19990730

PRIORITY APPLN. INFO.: US 1997-36594 P 19970131
WO 1998-US1880 W 19980129

AB This invention provides sol. CTLA4 mutant mols. which bind with greater avidity to the CD86 antigen than wild type CTLA4. The sol. CTLA4 and its fusion protein with Ig. const. region are useful for treating immune diseases or inhibiting graft vs. host disease.

IC ICM A61K038-16
ICS C12P021-02; C12N015-00; C12N015-01; C12N015-09; C12N015-12; C12N015-63; C12N015-70; C12N015-79; C07K014-705; C07H021-04
CC 15-2 (Immunochemistry)
Section cross-reference(s): 3
ST soluble CTLA4 **Ig** immune disease
IT CD28 (antigen)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**complex** with **Ig.**; sol. CTLA4 mutant **mols**. or **fusion proteins** for treating immune diseases or preventing graft vs. host disease)
IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(const. region; sol. CTLA4 mutant mols. or fusion proteins for treating immune diseases or preventing graft vs. host disease)

L34 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:527348 HCAPLUS
DOCUMENT NUMBER: 129:157691
TITLE: Recombinant preparation of chimeric protein **heterodimer** complexes comprised of integrin-**immunoglobulin** (**Ig**) and use as substitute for platelet
INVENTOR(S): Kainoh, Mie; Tanaka, Toshiaki

PATENT ASSIGNEE(S): Toray Industries, Inc., Japan
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9832771	A1	19980730	WO 1998-JP370	19980129
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2250291	AA	19980730	CA 1998-2250291	19980129
EP 896002	A1	19990210	EP 1998-901043	19980129
R: DE, FR, GB, IT				

PRIORITY APPLN. INFO.: JP 1997-15118 19970129
JP 1997-234544 19970829
WO 1998-JP370 19980129

AB Disclosed is an integrin-Ig chimeric protein heterodimer complex in which the .alpha.-chain and .beta.-chain of integrins have been assocd. in a stable state. The complex is formed by a chimeric protein of integrin .alpha. or .beta. chain-Ig H chain and a chimeric protein of integrin .alpha. or .beta. chain-Ig L chain. Also described is the use of the complex as a drug; or as a reagent for the assay of binding of integrins to ligands, for the detection of substances binding to integrins or those inhibiting the binding of integrins to ligands. The complex is also usable as a diagnostic agent. It may also be used as a substitute for platelet that functions as an extracellular matrix receptor. Prepn. of expression plasmids for chimeric integrin .alpha.4-IgG H chain and chimeric integrin .beta.1-IgG H chain of human, resp., co-expression of the 2 chimeric proteins in transgenic CHO cells, and characterization of the chromatog.-purified heterodimer complexes were shown.

IC ICM C07K014-705
ICS C12N015-12; G01N033-50
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 13, 14
ST chimeric protein **heterodimer** complex integrin **Ig**; platelet substitute integrin **Ig** chimeric complex; therapeutic diagnostic integrin **Ig** chimeric complex
IT **Molecular** cloning
(**chimeric** gene for **chimeric protein heterodimer complexes** comprised of integrin .alpha.2 or .alpha.4 or .beta.1 and IgG1 .gamma.1 chain of human)
IT Protein receptors
RL: PRP (Properties)
(extracellular matrix-assocd. protein; chimeric protein **heterodimer** complexes comprised of integrin-**Ig** as)
IT DNA sequences
(for chimeric protein **heterodimer** complexes comprised of integrin .alpha.2 or .alpha.4 or .beta.1 and IgG1 .gamma.1 chain of human)
IT CD11b (antigen)
CD11c (antigen)
Integrin .alpha.IIb
Integrin .alpha.v
Integrin .alpha.1
Integrin .alpha.2
Integrin .alpha.3
Integrin .alpha.4

Integrin .alpha.5
Integrin .alpha.6
Integrin .beta.1
Integrin .beta.2
Integrin .beta.3
Integrin .beta.4
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(fusion protein with Igs; recombinant prepn. of chimeric protein **heterodimer** complexes comprised of integrin-**Ig** and use as substitute for platelet)

IT IgG1
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(fusion protein with integrins; recombinant prepn. of chimeric protein **heterodimer** complexes comprised of integrin-**Ig** and use as substitute for platelet)

IT CD antigens
Integrins
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(integrin .alpha.7, fusion protein with Igs; recombinant prepn. of chimeric protein **heterodimer** complexes comprised of integrin-**Ig** and use as substitute for platelet)

IT CD antigens
Integrins
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(integrin .beta.5, fusion protein with Igs; recombinant prepn. of chimeric protein **heterodimer** complexes comprised of integrin-**Ig** and use as substitute for platelet)

IT CD antigens
Integrins
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(integrin .beta.7, fusion protein with Igs; recombinant prepn. of chimeric protein **heterodimer** complexes comprised of integrin-**Ig** and use as substitute for platelet)

IT Protein sequences
(of chimeric protein **heterodimer** complexes comprised of integrin .alpha.2 or .alpha.4 or .beta.1 and IgG1 .gamma.1 chain of human)

IT Diagnostic agents
Drugs
Platelet (blood)
(recombinant prepn. of chimeric protein **heterodimer** complexes comprised of integrin-**Ig** and use as substitute for platelet)

IT CD11a (antigen)
Integrins
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(recombinant prepn. of chimeric protein **heterodimer** complexes comprised of integrin-**Ig** and use as substitute for platelet)

IT Fusion proteins (chimeric proteins)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(recombinant prepn. of chimeric protein **heterodimer** complexes comprised of integrin-**Ig** and use as substitute for platelet)

IT **Immunoglobulin** heavy chains

Immunoglobulin light chains
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(recombinant prepn. of chimeric protein **heterodimer** complexes comprised of integrin-**Ig** and use as substitute for platelet)

IT Integrins
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(.alpha.8; fusion protein with Igs; recombinant prepn. of chimeric protein **heterodimer** complexes comprised of integrin-**Ig** and use as substitute for platelet)

IT Integrins
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(.alpha.9; fusion protein with Igs; recombinant prepn. of chimeric protein **heterodimer** complexes comprised of integrin-**Ig** and use as substitute for platelet)

IT Integrins
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(.beta.8; fusion protein with Igs; recombinant prepn. of chimeric protein **heterodimer** complexes comprised of integrin-**Ig** and use as substitute for platelet)

IT Integrins
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(.beta.6, fusion protein with Igs; recombinant prepn. of chimeric protein **heterodimer** complexes comprised of integrin-**Ig** and use as substitute for platelet)

IT 210974-89-3P 210974-91-7P 210974-93-9P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; recombinant prepn. of chimeric protein **heterodimer** complexes comprised of integrin-**Ig** and use as substitute for platelet)

IT 210974-88-2P 210974-90-6P 210974-92-8P
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; recombinant prepn. of chimeric protein **heterodimer** complexes comprised of integrin-**Ig** and use as substitute for platelet)

L34 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:388609 HCAPLUS
DOCUMENT NUMBER: 129:40132
TITLE: Recombinant LAG-3 protein derivatives and their use as **immunomodulators**
INVENTOR(S): El Tayar, Nabil; Mastrangeli, Renato; Huard, Bertrand; Triebel, Frederic
PATENT ASSIGNEE(S): Institut Gustave Roussy, Fr.; Institut National De La Sante Et De La Recherche Medicale (INSERM); Applied Research Systems ARS Holding N.V.; El Tayar, Nabil; Mastrangeli, Renato; Huard, Bertrand; Triebel, Frederic
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9823741	A1	19980604	WO 1997-FR2126	19971125
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9852294	A1	19980622	AU 1998-52294	19971125
AU 728911	B2	20010118		
EP 942973	A1	19990922	EP 1997-947136	19971125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2000516101	T2	20001205	JP 1998-524362	19971125

PRIORITY APPLN. INFO.: FR 1996-14608 A 19961128
WO 1997-FR2126 W 19971125

AB The invention concerns a purified polypeptide corresponding to a mutated form of the sol. LAG-3 protein or of one of its fragments comprising the extracellular domain D1 and D2. These proteins may be produced with recombinant organisms and may be used as immunomodulators, e.g., to treat autoimmune diseases and organ transplant rejection and for anti-cancer immunotherapy. Numerous mutants of the 149-amino acid protein comprising the D1 and D2 domains of the LAG-3 protein were produced in COS7 cells and the effect of the mutations on binding to Daudi cells analyzed. Some mutations increased interaction while others diminished the binding. One set of mutations not only inhibited interaction of LAG-3 with MHCII on the Daudi cells, but also interfered with LAG-3 homo-oligomerization.

IC ICM C12N015-12
ICS C07K014-705; A61K038-17; C12N015-62; C07K016-46; C12N001-21; C12N005-10; C12N001-21; C12R001-19

CC 15-2 (Immunochemistry)
Section cross-reference(s): 1, 3

ST LAG3 protein mutant recombinant **immunomodulator**

IT Genes (animal)
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(LAG-3; recombinant LAG-3 protein derivs. and their use as **immunomodulators**)

IT Class II **MHC** antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(LAG3 binding to, modulation of; recombinant LAG-3 protein derivs. and their use as **immunomodulators**)

IT Immunotherapy
(anti-cancer; recombinant LAG-3 protein derivs. and their use as **immunomodulators**)

IT COS-7 cell
(cloning/expression in; recombinant LAG-3 protein derivs. and their use as **immunomodulators**)

IT IgG1
Immunoglobulins
Radionuclides
Toxins
RL: BPN (Biosynthetic preparation); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(**fusion** products with LAG-3 derivs.; recombinant LAG-3 **protein** derivs. and their use as **immunomodulators**)

IT Molecular association
(of MHCII and LAG3, modulation of; recombinant LAG-3 protein derivs. and their use as **immunomodulators**)

IT **Immunomodulators**
Molecular cloning
(recombinant LAG-3 protein derivs. and their use as **immunomodulators**)

IT Transplant (organ)
(rejection of, treatment of; recombinant LAG-3 protein derivs. and their use as **immunomodulators**)

IT Autoimmune diseases
(treatment of; recombinant LAG-3 protein derivs. and their use as **immunomodulators**)

IT 208411-18-1P 208411-19-2P 208411-20-5P 208411-21-6P 208411-22-7P
208411-23-8P 208411-24-9P 208411-25-0P 208411-26-1P 208411-27-2P
208411-28-3P 208411-29-4P
RL: BPN (Biosynthetic preparation); BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(amino acid sequence; recombinant LAG-3 protein derivs. and their use as **immunomodulators**)

L34 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:126278 HCAPLUS
DOCUMENT NUMBER: 128:191578
TITLE: Soluble monovalent and **multivalent** **MHC** class II **fusion proteins** , and uses therefor
INVENTOR(S): Wucherpfennig, Kai W.; Strominger, Jack L.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA; Wucherpfennig, Kai W.; Strominger, Jack L.
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9806749	A2	19980219	WO 1997-US14503	19970815
W: AU, CA, JP, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9740723	A1	19980306	AU 1997-40723	19970815
AU 730457	B2	20010308		
EP 935607	A2	19990818	EP 1997-938386	19970815
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000516470	T2	20001212	JP 1998-510100	19970815
PRIORITY APPLN. INFO.:			US 1996-24077 P	19960816
			WO 1997-US14503 W	19970815

AB The present invention is directed to the design, prodn., and use of recombinant fusion proteins derived, in part, from the proteins of the human Major Histocompatibility Complex. The MHC II fusion proteins are useful for treating autoimmune diseases, e.g. multiple sclerosis or rheumatoid arthritis. The MHC class II includes HLA-DR1, HLA-DR2, HLA-DR4, HLA-DQ1, HLA-DQ2, and HLA-DQ8 .alpha. chain or .beta. chain. Thus, DRA*0101 extracellular region-Fos leucine zipper domain and

DRB1*1501 extracellular region-Jun leucine zipper domain fusion proteins, HLA-DR2 **heterodimers** (both DR.alpha. and DR.beta.), DR2-IgG fusion protein, and DR2-IgM fusion protein were prepd. The prepd. DR2-Ig. fusion proteins were used for selective depletion of T cells, or were complexed to toxins for inducing apoptosis of selective T cells.

IC ICM C07K014-00

CC 15-2 (Immunochemistry)
Section cross-reference(s): 3

ST **MHC** class II **Ig fusion protein**

IT Flow cytometry
(FACS (fluorescence-activated cell sorting); sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT HLA-DQ antigen
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DQ1 antigen, **fusion proteins**; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT HLA-DQ antigen
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DQ2 antigen, **fusion proteins**; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT HLA-DQ antigen
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DQ8 antigen, **fusion proteins**; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT Genes (animal)
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DQA1, **fusion proteins**; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT Genes (animal)
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DQB1, **fusion proteins**; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT Genes (animal)
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DRA, **fusion proteins**; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT Genes (animal)
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-DRB, **fusion proteins**; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT **Fusion proteins** (**chimeric proteins**)
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**MHC** II; sol. monovalent and **multivalent**

MHC class II **fusion proteins** for treating autoimmune diseases)

IT Apoptosis
(T cell; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT **Immunity**
(adoptive; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugate; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT **Immunoglobulin** heavy chains
Immunoglobulin light chains
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(const. region **fusion proteins**; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT T cell (lymphocyte)
(depletion; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT Class II **MHC** antigens
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**fusion protein**; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT HLA-DR1 antigen
HLA-DR2 antigen
HLA-DR4 antigen
IgA
IgD
IgE
IgG
IgG2a
IgM
c-fos gene (animal)
c-jun gene (animal)
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**fusion proteins**; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT Skin diseases
(pemphigus vulgaris; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT Autoimmune diseases
Leucine zipper
Multiple sclerosis
Rheumatoid arthritis
Systemic lupus erythematosus
(sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT **Immunoglobulin fusion** products

RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT TCR (T cell receptors)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT Myelin basic **protein**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT 203592-10-3 203592-12-5
RL: PRP (Properties)
(amino acid sequence; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

IT 203592-09-0 203592-11-4 203592-13-6 203592-14-7
RL: PRP (Properties)
(nucleotide sequence; sol. monovalent and **multivalent MHC** class II **fusion proteins** for treating autoimmune diseases)

L34 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:89273 HCAPLUS
DOCUMENT NUMBER: 128:162875
TITLE: A multivalent major **histocompatibility** complex peptide **fusion protein** for modulating specific T cell function
INVENTOR(S): Hirsch, Raphael; Cullen, Constance M.
PATENT ASSIGNEE(S): Children's Hospital Medical Center, USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9803552	A2	19980129	WO 1997-US12324	19970715
WO 9803552	A3	19980625		
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6211342	B1	20010403	US 1996-683409	19960718
AU 9736645	A1	19980210	AU 1997-36645	19970715
EP 914347	A2	19990512	EP 1997-933467	19970715
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6197302	B1	20010306	US 1997-914421	19970819
PRIORITY APPLN. INFO.:			US 1996-683409 A	19960718
			WO 1997-US12324 W	19970715

AB The present invention describes a sol. fusion protein composed of a plurality of major histocompatibility complex (MHC) mols. linked together by a stabilizing structure herein referred to as the "linker", the MHC mols. being loaded with a specific peptide or peptides. Such fusion proteins, when linked to a second protein delivering a second signal, can be used as a method for stimulating or inhibiting specific T cell clones expressing T cell receptors (TCR) restricted to the specific MHC-peptide combination. The fusion proteins, when not linked to a second protein

delivering a second signal, can be used as a method for inhibiting specific T cell clones expressing TCR restricted to the specific MHC-peptide combination. Finally, the fusion proteins linked to a toxic protein such as ricin or diphtheria toxin can be used to destroy specific T cell clones expressing TCR restricted to the specific MHC-peptide combination. Such fusion proteins can thus be used as delivery systems to stimulate T cell immunity and as a treatment for diseases such as transplant rejection or autoimmunity. A divalent Kb-IgG1 fusion protein was prepd. Immobilized ova peptide-loaded fusion protein activated T cell hybridoma B3.645 in a peptide-specific, MHC-restricted manner. The sol. ova peptide-loaded fusion protein inhibited secretion of interleukin-2 from B3.645 cells in response to ova-loaded antigen-presenting cells. Addnl., the sol. fusion protein suppressed skin allograft rejection.

IC ICM C07K019-00
ICS C07K014-705; C07K016-00; A61K039-00; C07K014-78

CC 1-7 (Pharmacology)

ST **MHC fusion protein** peptide immunostimulant immunosuppressant

IT **Proteins**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(DNA-binding; zinc finger-contg., **linker**; multivalent major **histocompatibility** complex peptide **fusion protein** for modulating specific T cell function)

IT **Histocompatibility** antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IAq, conjugates, complexes with peptides; multivalent major **histocompatibility** complex peptide **fusion protein** for modulating specific T cell function)

IT Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antigenic, complexes with **MHC** conjugates; multivalent major **histocompatibility** complex peptide **fusion protein** for modulating specific T cell function)

IT Diphtheria toxin
Ricins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates with **MHC** conjugates; multivalent major **histocompatibility** complex peptide **fusion protein** for modulating specific T cell function)

IT Class II **MHC** antigens
H-2Kb antigen
HLA-A antigen
HLA-B antigen
HLA-C antigen
HLA-DP antigen
HLA-DQ antigen
HLA-DR antigen
MHC antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, complexes with peptides; multivalent major **histocompatibility** complex peptide **fusion protein** for modulating specific T cell function)

IT DNA-binding **proteins**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(leucine zipper-contg., **linker**; multivalent major **histocompatibility** complex peptide **fusion protein** for modulating specific T cell function)

IT CD28 (antigen)

LFA-1 (antigen)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ligand for, conjugates with **MHC** conjugates; multivalent major **histocompatibility** complex peptide **fusion protein** for modulating specific T cell function)

IT IgA
IgD
IgE
IgG
IgG1
IgG3
IgM
Immunoglobulins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**linker**; multivalent major **histocompatibility** complex peptide **fusion protein** for modulating specific T cell function)

IT Cytotoxic T cell
Immunostimulants
Immunosuppressants
Implants (drug delivery systems)
T cell (lymphocyte)
(multivalent major **histocompatibility** complex peptide **fusion protein** for modulating specific T cell function)

IT Bacteria (Eubacteria)
Fungi
Virus
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide antigens of, complexes with **MHC** conjugates; multivalent major **histocompatibility** complex peptide **fusion protein** for modulating specific T cell function)

IT Autoantigens
Tumor-associated antigen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptides, complexes with **MHC** conjugates; multivalent major **histocompatibility** complex peptide **fusion protein** for modulating specific T cell function)

IT Allograft
(suppression of rejection of; multivalent major **histocompatibility** complex peptide **fusion protein** for modulating specific T cell function)

IT Transplant rejection
(suppression of; multivalent major **histocompatibility** complex peptide **fusion protein** for modulating specific T cell function)

IT TCR (T cell receptors)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(targeting of; multivalent major **histocompatibility** complex peptide **fusion protein** for modulating specific T cell function)

L34 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:684303 HCAPLUS
DOCUMENT NUMBER: 127:358050
TITLE: Novel product and process for T lymphocyte veto
INVENTOR(S): Staerz, Uwe D.
PATENT ASSIGNEE(S): National Jewish Center for Immunology and Respiratory

Medicine, USA; Staerz, Uwe D.
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9737687	A1	19971016	WO 1997-US5943	19970410
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6060054	A	20000509	US 1996-630172	19960410
CA 2251819	AA	19971016	CA 1997-2251819	19970410
AU 9727258	A1	19971029	AU 1997-27258	19970410
EP 929316	A1	19990721	EP 1997-921134	19970410
R: CH, DE, FR, GB, IT, LI, SE				
US 6264950	B1	20010724	US 1999-375419	19990817

PRIORITY APPLN. INFO.: US 1996-630172 A2 19960410
WO 1997-US5943 W 19970410

AB The present invention relates to a product and process for suppressing an immune response using a T lymphocyte veto mol. capable of blocking cell surface mols. responsible for T cell activation. Disclosed is a CD4 or CD2 mol., assocd. with an Ig mol. capable of binding to a major histocompatibility antigen. The CD2 or CD4 mol. may also be replaced by CTLA4, Fas ligand, CD5, CD7, CD9, CD11, CD18, CD27, CD43, CD45. CD48, B7.1 or B7.2 protein. Also disclosed is a method to produce a T lymphocyte veto mol., a therapeutic compn. comprising a T lymphocyte veto mol. and methods to use T lymphocyte veto mols. in therapeutic processes requiring suppression of an immune response.

IC ICM A61K039-395
ICS C12N005-10; C12N015-12; C12N015-13; C12P021-08
CC 15-2 (Immunochemistry)
ST immunosuppressant **chimeric protein** T lymphocyte veto; CD2 CD4 **fusion protein** immunosuppression transplant

IT CD antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD11, **fusion protein; chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT CD antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD27, **fusion protein; chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(CD48 **fusion protein; chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT CD antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD9, **fusion protein; chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT **Proteins** (specific **proteins** and subclasses)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LMA, **fusion protein** contg.; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Epitopes
(**MHC** complex; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT **Proteins** (specific **proteins** and subclasses)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(RCA **fusion protein; chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT **Proteins** (specific **proteins** and subclasses)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SU (surface), **fusion protein** contg.; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Integrins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antigens CD11, **fusion protein; chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bile acid, **fusion protein** contg.; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Addison's disease
Affinity chromatography
Autoimmune diseases
Autoimmune thyroiditis
Autoimmunity
CD4-positive T cell
Celiac disease
Electrophoresis
Gel permeation chromatography
Graves' disease
Inhalants (drug delivery systems)
Insulin dependent diabetes mellitus
Intravenous injections
Islet of Langerhans

Multiple sclerosis
Myasthenia gravis
Nasal drug delivery systems
Oral drug delivery systems
Protein sequences
Reversed phase chromatography
Rheumatoid arthritis
Systemic lupus erythematosus
Topical drug delivery systems
Transdermal drug delivery systems
Transplant (organ)
Transplant rejection
(**chimeric proteins** contg. CD2 or CD4 and **Ig**
. for T lymphocyte veto or immunosuppression)

IT **Fusion proteins** (**chimeric proteins**
)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**chimeric proteins** contg. CD2 or CD4 and **Ig**
. for T lymphocyte veto or immunosuppression)

IT Class I **MHC** antigens
MHC antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**chimeric proteins** contg. CD2 or CD4 and **Ig**
. for T lymphocyte veto or immunosuppression)

IT Blood **proteins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**chimeric proteins** contg. CD2 or CD4 and **Ig**
. for T lymphocyte veto or immunosuppression)

IT Liquid chromatography
(focusing; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**fusion protein** contg. tissue-specific; **chimeric proteins** contg. CD2 or CD4 and **Ig**.
for T lymphocyte veto or immunosuppression)

IT Asialoglycoprotein receptors
c-Kit (**protein**)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**fusion protein** contg.; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Growth factors (animal)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**fusion protein** contg.; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Baboon
Cat (Felis catus)
Cattle
Dog (Canis familiaris)
Goat
Hamster
Horse (Equus caballus)
Mouse

Myocyte (heart)
Rabbit
Rat
Swine
(**fusion protein; chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT CD2 (antigen)
CD28 (antigen)
CD4 (antigen)
CD45 (antigen)
CD5 (antigen)
CD7 (antigen)
CD80 (antigen)
CD86 (antigen)
CTLA-4 (antigen)
Fas ligand
IgG2a
Immunoglobulins
Integrin .beta.2
Leukosialin
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**fusion protein; chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Injections (drug delivery systems)
Solutions (drug delivery systems)
(i.p. solns.; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Drug delivery systems
(intraarticular; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Drug delivery systems
(intracranial; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Primate
(non-human **fusion protein; chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Bile acids
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(receptor, **fusion protein** contg.; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Animal cell line
(recombinant T; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT B cell (lymphocyte)
(recombinant cell line; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Epithelium
Neurons
(recombinant cell; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

IT Fibroblast
Hematopoietic stem cell

(recombinant; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)
IT Drug delivery systems
(rectal; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)
IT Heart diseases
(rheumatoid carditis; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)
IT T cell (lymphocyte)
(veto mol.; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)
IT 1306-06-5, Hydroxyapatite
RL: BUU (Biological use, unclassified); DEV (Device component use); BIOL (Biological study); USES (Uses)
(adsorption; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)
IT 132729-32-9, Antigen B 7 (mouse clone pB7 precursor **protein** moiety reduced) 198651-08-0 198651-09-1 198651-10-4 198652-30-1 198652-31-2 198652-32-3 198652-33-4 198652-34-5 198652-35-6, CD5 (antigen) (human fragment) 198652-36-7 198652-37-8 198652-38-9 198652-39-0 198652-40-3 198652-41-4 198652-42-5 198652-43-6 198652-44-7 198652-45-8 198652-46-9
RL: PRP (Properties)
(amino acid sequence; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)
IT 68181-17-9
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as **linker**; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)
IT 9002-60-2, Corticotropin, biological studies 9002-71-5, Thyroid stimulating hormone 11000-17-2, Vasopressin
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**chimeric** immunosuppressing **protein** contg.; **chimeric proteins** contg. CD2 or CD4 and **Ig**. for T lymphocyte veto or immunosuppression)

L34 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:650464 HCAPLUS
DOCUMENT NUMBER: 127:306596
TITLE: Soluble recombinant divalent and **multivalent heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and fusion products with **immunoglobulins**
INVENTOR(S): Schneck, Jonathan P.; O'Herrin, Sean
PATENT ASSIGNEE(S): ohns Hopkins University, USA; Schneck, Jonathan P.; O'Herrin, Sean
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9735991	A1	19971002	WO 1997-US4694	19970328

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC,

LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,
ML, MR, NE, SN, TD, TG

CA 2250166	AA	19971002	CA 1997-2250166	19970328
AU 9724224	A1	19971017	AU 1997-24224	19970328
AU 729406	B2	20010201		
EP 889964	A1	19990113	EP 1997-919902	19970328
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11507843	T2	19990713	JP 1997-534519	19970328
KR 2000005060	A	20000125	KR 1998-7687	19980928

PRIORITY APPLN. INFO.: US 1996-14367 P 19960328
WO 1997-US4694 W 19970328

AB Specificity in immune responses is in part controlled by the selective interaction of T cell receptors with their cognate ligands, peptide/MHC mols. The discriminating nature of this interaction makes these mols., in sol. form, good candidates for selectively regulating immune responses. Attempts to exploit sol. analogs of these proteins has been hampered by the intrinsic low avidity of these mols. for their ligands. To increase the avidity of sol. analogs for their cognates to biol. relevant levels, divalent peptide/MHC complexes or T cell receptors (superdimers) were constructed. Using a recombinant DNA strategy, DNA encoding either the MHC class II/peptide or TCR **heterodimers** was ligated to DNA coding for murine Ig heavy and light chains. These constructs were subsequently expressed in a baculovirus expression system. Enzyme-linked immunosorbent assays (ELISA) specific for the Ig and polymorphic determinants of either the TCR or MHC fraction of the mol. indicated that infected insect cells secreted approx. 1 .mu.g/mL of sol., conformationally intact chimeric superdimers. The results of flow cytometry demonstrated that the TCR and class II chimeras bound specifically with high avidity to cells bearing their cognate receptors. These superdimers will be useful for studying TCR/MHC interactions, lymphocyte tracking, identifying new antigens, and have possible uses as specific regulators of immune responses.

IC ICM C12N015-62
ICS C07K019-00; C12N005-10; A61K039-00; A61K038-17; G01N033-68; G01N033-574; G01N033-569; G01N033-543; C07K014-74; C07K014-705; C07K016-00

CC 15-1 (Immunochemistry)
Section cross-reference(s): 1, 3

ST recombinant **Ig** fusion product immunoassay immunosuppressant; T cell receptor fusion **Ig** recombinant; TCR receptor fusion **Ig** recombinant use; antigen **MHC** peptide fusion **Ig** recombinant

IT Carbohydrates, biological studies
Glycoproteins (general), biological studies
Proteins (general), biological studies
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**Ig** binding by; sol. recombinant divalent and **multivalent heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and **fusion** products with Igs)

IT **Chimeric** genes
RL: ARU (Analytical role, unclassified); BPR (Biological process); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)

(**Ig-protein**; sol. recombinant divalent and **multivalent heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and **fusion** products with Igs)

IT T cell activation
(antigen-specific; sol. recombinant divalent and **multivalent heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and fusion products with Igs)

IT Peptides, biological studies
RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(complexes, with **MHC**; sol. recombinant divalent and **multivalent heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and fusion products with Igs)

IT **MHC** antigens
RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(complexes, with peptides; sol. recombinant divalent and **multivalent heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and fusion products with Igs)

IT Immunoassay
(for antigens; sol. recombinant divalent and **multivalent heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and fusion products with Igs)

IT Transplant (organ)
(foreign antigen; sol. recombinant divalent and **multivalent heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and fusion products with Igs)

IT Antigens
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(foreign transplantation antigens; sol. recombinant divalent and **multivalent heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and fusion products with Igs)

IT Class II **MHC** antigens
IgA
IgD
IgE
IgG1
IgG2a
IgG2b
IgG3
IgM
TCR (T cell receptors)
RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fusion products; sol. recombinant divalent and **multivalent heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and fusion products with Igs)

IT **Immunity**
(**immune** recognition; sol. recombinant divalent and **multivalent heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and fusion products with Igs)

IT Immobilization (**molecular**)
(of recombinant **protein**; sol. recombinant divalent and **multivalent heterodimeric** peptide/**MHC** antigen **complexes** or T cell receptors and **fusion**

products with Igs)
IT Autoimmune diseases
Drug carriers (drug delivery systems)
Gene therapy
Genetic vectors
Immunosuppressants
Immunotherapy
Molecular cloning
Mouse
Quaternary structure (**protein**)
(sol. recombinant divalent and **multivalent** **heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and **fusion** products with Igs)
IT Tumor-associated antigen
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(sol. recombinant divalent and **multivalent** **heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and fusion products with Igs)
IT **Fusion proteins** (**chimeric proteins**)
Immunoglobulin fusion products
RL: ARU (Analytical role, unclassified); BPN (Biosynthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sol. recombinant divalent and **multivalent** **heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and **fusion** products with Igs)
IT Lymphocyte
(tracking; sol. recombinant divalent and **multivalent** **heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and fusion products with Igs)
IT Antigens
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(virus-assocd.; sol. recombinant divalent and **multivalent** **heterodimeric** peptide/**MHC** antigen complexes or T cell receptors and fusion products with Igs)

L34 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:672512 HCAPLUS
DOCUMENT NUMBER: 125:326396
TITLE: Redirection of cellular **immunity** by receptor chimeras
INVENTOR(S): Seed, Brian; Romeo, Charles; Kolanus, Waldemar
PATENT ASSIGNEE(S): General Hospital Corporation, USA
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9625953	A1	19960829	WO 1996-US1056	19960125
W: AU, CA, CZ, FI, HU, JP, KR, NO, NZ, RU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2209300	AA	19960829	CA 1996-2209300	19960125
AU 9648588	A1	19960911	AU 1996-48588	19960125

AU 708339 B2 19990805
EP 871495 A1 19981021 EP 1996-904498 19960125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE
JP 11505409 T2 19990521 JP 1996-525685 19960125
FI 9703437 A 19971016 FI 1997-3437 19970821
NO 9703864 A 19971022 NO 1997-3864 19970822
PRIORITY APPLN. INFO.: US 1995-394176 19950224
WO 1996-US1056 19960125

AB Disclosed is a method of directing a cellular response in a mammal by expressing in a cell of the mammal at least two chimeric receptors which trigger the specific recognition and destruction of an infective agent, a cell infected with an infective agent, a tumor or cancerous cell, or an autoimmune-generated cell. One of the expressed chimeric receptors includes an extracellular portion which is capable of specifically recognizing and binding the target cell or target infective agent and an intracellular or **transmembrane** portion which is capable of signalling the therapeutic cell to destroy a receptor-bound target cell or a receptor-bound target infective agent; and the second chimeric receptor includes an extracellular portion which is capable of specifically recognizing and binding the target cell or target infective agent and an intracellular portion which is derived from CD28. The extracellular portion comprises an HIV envelope-binding portion of CD4, or an extracellular portion of CD16, CD7 and CD5; and the intracellular portion comprises a signal transducing portion of T cell receptor, B cell receptor, or Fc receptor. Also disclosed are pairs of useful chimeric receptors, cells which express the chimeric receptors, and DNA encoding the chimeric receptors.

IC ICM A61K048-00
ICS C12N005-00; C07K014-705; C12N015-12
CC 15-1 (Immunochemistry)
ST chimeric receptor **immune** cell cancer autoimmune

IT Autoimmune disease
(-generated cells; therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT **Proteins**, specific or class, biological studies
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(T3 gamma; therapeutic cells expressing **chimeric** receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Vaccinia
(infection; therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Acquired **immune** deficiency syndrome
Deoxyribonucleic acid sequences
HeLa cell
Infection
Macrophage
Mast cell
Neoplasm
Neutrophil
Protein sequences
(therapeutic cells expressing **chimeric** receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Deoxyribonucleic acids
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Animal cell
(therapeutic; therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Antigen receptors
Receptors
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(BCR (B-cell antigen receptors), mb1 or B29; therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD28, therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD3, .delta.; therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD4, therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD5, therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD7, therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT **Immunoglobulin** receptors
Receptors
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(FcR (**Ig** fragment Fc receptor), .gamma.; therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT **Immunoglobulin** receptors
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Fc.gamma.RII-C (IgG fragment Fc receptor II C), human; therapeutic

cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Receptors
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Fc.gamma.RII-C, (IgG fragment Fc receptor II C), human; therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT **Immunoglobulin** receptors
Receptors
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Fc.gamma.RIIA (IgG fragment Fc receptor IIA), human; therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT **Immunoglobulin** receptors
Receptors
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Fc.gamma.RIII (IgG fragment Fc receptor III), human; therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT **Immunoglobulins**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(G1, chimeric receptor contg.; therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT **Histocompatibility** antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**MHC** (major **histocompatibility** complex), therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Lymphocyte
(T-cell, therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Lymphocyte
(T-cell, cytotoxic, therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Antigen receptors
Receptors
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TCR (T-cell antigen receptor), .zeta. and .eta.; therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT **Immunity**
(cell-mediated, therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Receptors
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(chimeric, therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT **Proteins**, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(envelope, HIV; therapeutic cells expressing **chimeric** receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Sialoglycoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gp120env, HIV; therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gp41env, therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Leukocyte
(granulocyte, therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Virus, animal
(human immunodeficiency, therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Virus, animal
(immunodeficiency, therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT **Proteins**, specific or class
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(membrane-assocd., **chimeric** receptor; therapeutic cells expressing **chimeric** receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Lymphocyte
(natural killer cell, therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT Embryo
(stem cell, therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT 146157-54-2, 31-142-Antigen CD 3 (human Jurkat cell .zeta.-chain **protein** moiety) 183131-47-7, Antigen CD 3 (human .eta.-chain fragment)
RL: PRP (Properties)
(amino acid sequence; therapeutic cells expressing **chimeric** receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT 183131-46-6
RL: PRP (Properties)
(nucleotide sequence; therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

IT 141923-04-8P 145385-04-2P 145385-05-3P 145385-06-4P 146157-55-3P
146157-56-4P 146157-57-5P 146157-59-7P 146157-60-0P 146157-61-1P

146157-62-2P 183023-47-4P 183023-52-1P, 137-195-Glycoprotein (mouse gene mb-1) 183023-53-2P 183023-54-3P 183079-30-3P
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic cells expressing chimeric receptor for redirecting cellular **immunity** to infectious agent or target cancer)

L34 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:494194 HCAPLUS
DOCUMENT NUMBER: 125:151112
TITLE: Targeting complexes for gene therapy
INVENTOR(S): Grosveld, Franklin Gerardus
PATENT ASSIGNEE(S): Medical Research Council, UK
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9619241	A1	19960627	WO 1995-GB2974	19951219
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9642684	A1	19960710	AU 1996-42684	19951219
EP 799057	A1	19971008	EP 1995-941199	19951219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
US 5849718	A	19981215	US 1995-574702	19951219
PRIORITY APPLN. INFO.:			GB 1994-25600	19941219
			WO 1995-GB2974	19951219

AB The invention relates to a compn. including a targeting complex contg. a component of an effector system and a ligand capable of targeting a cell surface marker in assocn. with at least one further targeting complex contg. a further component of the effector system and a ligand capable of targeting a cell surface marker which is a different cell surface marker to that targeted by at least one of the other targeting complexes, wherein the desired activity of the effector system is dependent on the selective internalization and functional cooperation of the components thereof. The components of the effector system comprise an effector DNA transcription unit and one or more regulators which modulate the expression of the effector DNA transcription unit.

IC ICM A61K047-48
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 1, 3
IT Ribonucleic acid formation factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Vmw65 (virion-assocd. stimulatory **protein**, 65,000-**mol**.-wt.), **fusion** products with Tet repressor gene; DNA targeting **complexes** for gene therapy)
IT **Immunoglobulins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabolic disorders, X-linked infantile hypogammaglobulinemia, DNA targeting complexes for gene therapy)

L34 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:345795 HCAPLUS
DOCUMENT NUMBER: 125:26231
TITLE: Cells bearing CD4 extracellular domain fusion products as decoys for the killing of HIV-1-infected cells
INVENTOR(S): Seed, Brian; Banapour, Babak; Romeo, Charles; Kolanus, Waldemar
PATENT ASSIGNEE(S): General Hospital Corporation, USA
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9603883	A1	19960215	WO 1995-US9468	19950726
W: AU, BR, BY, CA, CN, CZ, FI, HU, JP, KR, MX, NO, NZ, PL, RU, SI, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5851828	A	19981222	US 1994-284391	19940802
AU 9532014	A1	19960304	AU 1995-32014	19950726
AU 697489	B2	19981008		
EP 781095	A1	19970702	EP 1995-928152	19950726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 10503932	T2	19980414	JP 1995-506600	19950726
PL 181085	B1	20010531	PL 1995-318443	19950726
FI 9700428	A	19970326	FI 1997-428	19970131
NO 9700440	A	19970326	NO 1997-440	19970131

PRIORITY APPLN. INFO.:

US 1994-284391	A	19940802
US 1995-394388	A	19950224
US 1991-665961	B2	19910307
US 1992-847566	B2	19920306
US 1994-195395	B2	19940214
WO 1995-US9468	W	19950726

AB Cells that carry a surface mol. that has the extracellular domain of the CD4 antigen fused to a **transmembrane** receptor are described for identification and killing of HIV-1-infected cells in the treatment of HIV-1 infection. The chimeric receptor is presented by a cell capable of killing bound cells, e.g. a cytotoxic T-lymphocyte or a natural killer cell, and the binding of the antigen activates the intracellular domain of the receptor that activates the cell to kill the infected cell. The CD4 antigen domain is linked to the intracellular domain of a receptor such as a T-cell receptor, a B-cell receptor, or an Fc receptor, preferably by an Ig hinge and CH2 and CH3 domains to ensure correct spacing of the domains. Cells that express these CD4 receptors and DNA and vectors encoding the receptors are described. Fusion proteins with the intracellular domains of the .zeta.-, .gamma.- and .eta.-chains of the T-cell receptor were synthesized in animal cell hosts where they were able to assoc. with the Fc.gamma.RIII receptor. These cells were able lyse cells presenting a gp120/gp41 complex.

IC ICM A01N063-00
ICS C12P021-06; C12N015-11; C12N015-63; C12N015-85; C07H021-04

CC 1-5 (Pharmacology)
Section cross-reference(s): 15

IT **Immunoglobulin** receptors
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(FcRII, fusion products with CD antigens, cytolytic signal transduction

by; cells bearing CD4 extracellular domain fusion products as decoys for killing of HIV-1-infected cells)

IT Antigens
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD34, fusion products with CD4 antigen and **immune** system receptors; cells bearing CD4 extracellular domain fusion products as decoys for killing of HIV-1-infected cells)

IT Antigens
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD5, fusion products with CD4 antigen and **immune** system receptors; cells bearing CD4 extracellular domain fusion products as decoys for killing of HIV-1-infected cells)

IT Antigens
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD7, fusion products with CD4 antigen and **immune** system receptors; cells bearing CD4 extracellular domain fusion products as decoys for killing of HIV-1-infected cells)

IT **Immunoglobulin** receptors
Receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(Fc.gamma.RIII (IgG fragment Fc receptor III), fusion products with T-cell receptor .zeta.-subunit do not bind CD3 antigens; cells bearing CD4 extracellular domain fusion products as decoys for killing of HIV-1-infected cells)

IT **Immunoglobulins**
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G1, fusion products with CD4 antigen and **immune** system receptors; cells bearing CD4 extracellular domain fusion products as decoys for killing of HIV-1-infected cells)

IT Receptors
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**Ig**, FcRII, fusion products wth CD antigens, cytolytic signal transduction by; cells bearing CD4 extracellular domain fusion products as decoys for killing of HIV-1-infected cells)

IT **Histocompatibility** antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**MHC** (major **histocompatibility** antigen complex), class II, CD4 fusion products not recognizing cells presenting; cells bearing CD4 extracellular domain fusion products as decoys for killing of HIV-1-infected cells)

IT Gene, animal
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**chimeric**, for **fusion proteins** of CD4 antigens and **immune** system receptors; cells bearing CD4 extracellular domain **fusion** products as decoys for killing of HIV-1-infected cells)

L34 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:113481 HCAPLUS
DOCUMENT NUMBER: 124:137837
TITLE: Host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities
INVENTOR(S): Young, Kathleen H.; Ozenberger, Bradley A.

PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9534646	A1	19951221	WO 1995-US6895	19950531
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, UG, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5989808	A	19991123	US 1994-259609	19940614
CA 2195083	AA	19951221	CA 1995-2195083	19950531
AU 9526066	A1	19960105	AU 1995-26066	19950531
AU 706173	B2	19990610		
EP 765389	A1	19970402	EP 1995-920689	19950531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
ZA 9504892	A	19960130	ZA 1995-4892	19950613
LT 4230	B	19971027	LT 1997-4	19970113
LV 11906	B	19980620	LV 1997-4	19970214
US 6251602	B1	20010626	US 1999-263944	19990308
US 6284519	B1	20010904	US 1999-305483	19990506

PRIORITY APPLN. INFO.: US 1994-259609 A 19940614
WO 1995-US6895 W 19950531

AB This invention relates to novel modified host cells which express heterologous fused proteins and methods of screening for test samples having peptide-binding activity; wherein the modified host cell comprises: (a) a gene sequence encoding a heterologous fusion protein; said fusion protein comprising a first peptide of a peptide binding pair, or segment of said first peptide, which is joined to either a DNA binding domain or its corresponding transcriptional activation domain of a transcriptional activation protein; (b) a gene sequence encoding a heterologous fusion protein, said fusion protein comprising a second peptide of the peptide binding pair in (a), or a segment thereof, fused to either a DNA binding domain or its corresponding transcriptional activation domain, whichever one is not employed in (a); (c) a reporter gene operatively assocd. with the transcriptional activation protein, or a portion thereof; (d) optionally, a deletion or mutation in the chromosomal DNA of the host cell for the transcriptional activation protein if present in the selected host cell.

IC ICM C12N015-00
ICS C12N001-19; C12N015-18; C12Q001-68; C12N015-62

CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 2, 9

ST **fusion protein** method screening receptor ligand; peptide binding screening host **fusion protein**

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Arg81, DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Ribonucleic acid formation factors

RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Sialoglycoproteins
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(VCAM (vascular cell adhesion mol.); host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Antigens
RL: MSC (Miscellaneous)
(antigen recognition or presentation mol.; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Plasmid and Episome
(autonomously-replicating; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT **Proteins**, specific or class
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(gene AIC2A, transducer; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Amphibian
Aspergillus
Eukaryote
Fungi
Immunomodulators
Mammal
Mutation
Neurospora
Pichia pastoris
Saccharomyces cerevisiae
Schizosaccharomyces pombe
Yeast
(host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Animal growth regulators
Fibrinogens
Fibronectins
Integrins
Interferons
Ligands
Lymphokines and Cytokines
Peptides, biological studies
Receptors
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Peptides, biological studies
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL

(Biological study); PROC (Process)
(insect differentiation; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT **Proteins**, specific or class
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(kh97, transducer; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT G **proteins** (guanine nucleotide-binding **proteins**)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ligands for G **protein**-coupled receptors; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Antibiotic resistance
(reporter gene conferring resistance; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Gene
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(reporter; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(ADR1 (alc. dehydrogenase II gene regulatory, 1), DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Antigen receptors
Receptors
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(BCR (B-cell antigen receptors), host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Glycoproteins, specific or class
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(CAM, host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Glycoproteins, specific or class
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(E-CAM, host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT **Immunoglobulin** receptors
Receptors
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)

(FcR (**Ig** fragment Fc receptor), host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Glycoproteins, specific or class
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(ICAM (intercellular adhesion mol.), host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT **Histocompatibility** antigens
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(**MHC** (major **histocompatibility** complex), host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Antigen receptors
Receptors
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(TCR (T-cell antigen receptor), host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Vmw65 (virion-assocd. stimulatory **protein**, 65,000-mol.-wt.), DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Animal growth regulators
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(blood platelet-derived growth factors, peptide ligand; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Animal growth regulators
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(ciliary neurotrophic factors, peptide ligand; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); BPR (Biological process); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(**fusion** products, host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT **Proteins**, specific or class
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(gene AIC2B, transducer; host cells transformed with **fusion protein** gene and method for screening test samples with

receptor-ligand interactions or peptide-binding activities)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene CUP2, DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene GAL4, DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene GCN4, DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene HAP1, DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene LAC9, DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene MCM1, DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene PPR1, DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene STE12, DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(gene SWI5, DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene lexA, DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene qa-1F, DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Glycoproteins, specific or class
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(gp130, transducer; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT **Proteins**, specific or class
RL: MSC (Miscellaneous)
(green fluorescent, reporter gene; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Hemopoietins
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(hematopoietic cell growth factors, host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Hemopoietins
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(hematopoietic cell growth factors KL, peptide ligand; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Lymphokines and Cytokines
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(interleukin 8, ligand for G-**protein** coupled receptor; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Lymphokines and Cytokines
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(interleukins, host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Animal
(invertebrate, ligands for invertebrate receptors; host cells transformed with **fusion protein** gene and method for

screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Gene, microbial
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(lacZ, reporter; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Lymphokines and Cytokines
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(leukemia-inhibiting factor, peptide ligand; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Glycoproteins, specific or class
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(selectins, host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT **Proteins**, specific or class
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(signal-transducing, host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Animal growth regulators
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(transforming growth factors, peptide ligand; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Lymphokines and Cytokines
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(tumor necrosis factor, peptide ligand; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT Ribonucleic acid formation factors
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(yAP-1 (yeast activator **protein** 1), DNA-binding or transcription-activating domain; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT 9002-62-4, Prolactin, biological studies 9002-72-6, Growth hormone 9004-10-8, Insulin, biological studies 61912-98-9, Insulin-like growth factor 137181-56-7, Systemin
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT 1393-25-5, Secretin 9002-67-9, LH 9002-68-0, Follicle stimulating hormone 9002-71-5, Thyrotropin 9007-92-5, Glucagon, biological studies

9034-39-3, Growth hormone releasing factor 37221-79-7, Vasoactive intestinal peptide
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(ligand for G-**protein** coupled receptor; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT 9054-75-5, Guanylate cyclase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ligands for guanylyl cyclase receptors; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT 79747-53-8, Tyrosine phosphatase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ligands for tyrosine phosphatase receptors; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT 9035-54-5, Placental lactogen 9061-61-4, Nerve growth factor 11096-26-7, Erythropoietin 62031-54-3, Fibroblast growth factor 62229-50-9, Epidermal growth factor 106956-32-5, Oncostatin m 127464-60-2, Vascular endothelial growth factor
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(peptide ligand; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

IT 9014-00-0, Luciferase 9040-07-7, Chloramphenicol acetyl transferase
RL: MSC (Miscellaneous)
(reporter gene; host cells transformed with **fusion protein** gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

L34 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:34810 HCAPLUS
DOCUMENT NUMBER: 124:84899
TITLE: Chimeric polypeptide for improvement of peptide delivery
INVENTOR(S): Cardy, Donald Leonard Nicholas; Carr, Frank Joseph
PATENT ASSIGNEE(S): Eclagen Ltd., UK
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9531483	A1	19951123	WO 1995-GB1107	19950515
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2190101	AA	19951123	CA 1995-2190101	19950515

AU 9524521	A1	19951205	AU 1995-24521	19950515
AU 701302	B2	19990121		
EP 759944	A1	19970305	EP 1995-918692	19950515
EP 759944	B1	20010816		
R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, NL, SE				
JP 10500670	T2	19980120	JP 1995-529465	19950515
AT 204300	E	20010915	AT 1995-918692	19950515

PRIORITY APPLN. INFO.: GB 1994-9643 A 19940513
GB 1994-17461 A 19940831
WO 1995-GB1107 W 19950515

AB Disclosed is a chimeric polypeptide comprising: a binding portion having specific binding affinity for a eukaryotic target cell surface component and an effector portion comprising an amino acid sequence capable of exerting a biol. effect. Binding of the polypeptide to the cell surface component induces internalization of at least the effector portion so as to allow the amino acid sequence to exert its biol. effect. A vaccine comprising the chimeric polypeptide of the invention, and a method of modulating the immune response of a human or animal subject are also included. In example, chimeric polypeptide contg. anti-MHC class II peptide and p53 or influenza A matrix protein peptide was prepd. and tested for cell lysis induction. Recombinant antibody specific for MBr1 antigen and p53 or influenza A matrix protein was also prepd. to induce cytotoxic T lymphocyte activity against MCF7 cells.

IC ICM C07K019-00
ICS A61K039-00

CC 15-2 (Immunochemistry)

IT **Immunoglobulin** receptors
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(FcRI; chimeric; chimeric polypeptide or recombinant bispecific antibody for improving peptide delivery and therapy)

IT Immunological accessory cell
Immunomodulators
Neoplasm
(chimeric polypeptide or recombinant bispecific antibody for improving peptide delivery and therapy)

IT Antigens
Immunoglobulins
Peptides, biological studies
Proteins, biological studies
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**chimeric**; **chimeric** polypeptide or recombinant bispecific antibody for improving peptide delivery and therapy)

IT Receptors
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**Ig**, FcRI; chimeric; chimeric polypeptide or recombinant bispecific antibody for improving peptide delivery and therapy)

IT **Histocompatibility** antigens
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**MHC** (major **histocompatibility** antigen complex), class I, chimeric; chimeric polypeptide or recombinant bispecific antibody for improving peptide delivery and therapy)

IT **Histocompatibility** antigens
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**MHC** (major **histocompatibility** antigen complex), class II, chimeric; chimeric polypeptide or recombinant bispecific

antibody for improving peptide delivery and therapy)

IT **Histocompatibility** antigens
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**MHC** (major **histocompatibility** complex), chimeric; chimeric polypeptide or recombinant bispecific antibody for improving peptide delivery and therapy)

IT **Proteins**, specific or class
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(matrix, **chimeric** influenza virus; **chimeric** polypeptide or recombinant bispecific antibody for improving peptide delivery and therapy)

L34 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:100384 HCAPLUS
DOCUMENT NUMBER: 118:100384
TITLE: Chimeric **immune** system receptors for use in the redirection of cellular **immunity**
INVENTOR(S): Seed, Brian; Romeo, Charles; Kolanus, Waldemar
PATENT ASSIGNEE(S): General Hospital Corp., USA
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9215322	A1	19920917	WO 1992-US1785	19920306
W: AU, BR, CA, CS, FI, HU, JP, KR, NO, PL, RU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9215559	A1	19921006	AU 1992-15559	19920306
AU 662136	B2	19950824		
EP 574512	A1	19931222	EP 1992-907958	19920306
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
BR 9205736	A	19940927	BR 1992-5736	19920306
JP 06509462	T2	19941027	JP 1992-507575	19920306
CZ 281881	B6	19970312	CZ 1993-1840	19920306
RU 2161044	C2	20001227	RU 1993-55035	19920306
HU 65631	A2	19940728	HU 1993-2524	19930306
HU 218732	B	20001128		
NO 9303169	A	19931104	NO 1993-3169	19930906
US 5843728	A	19981201	US 1995-417495	19950405
AU 9530328	A1	19960111	AU 1995-30328	19950830
AU 689289	B2	19980326		

PRIORITY APPLN. INFO.:

US 1991-665961	A	19910307
US 1992-847566	B1	19920306
WO 1992-US1785	A	19920306
US 1994-203866	B1	19940228

AB Fusion proteins of the intracellular domains of receptors such as the T-cell receptor and an heterologous ligand-binding domain are used to modulate the immunol. behavior of the domains. By using the antigen-recognition domain of an antibody, the response of T-cells to the cognate antigen can be stimulated. Chimeric genes encoding fusion proteins of the **transmembrane** regions of human Ig heavy chain and intracellular domains of the .zeta., .gamma., or .eta. subunits of the CD4 receptor were constructed and expressed in T-lymphocyte-derived cells using a vaccinia virus expression vector. Interaction of .zeta.-subunit

fusion proteins with other subunits of the receptor was controlled by substitution of an essential Asp or Cys in the intermembrane domain. When these proteins were capable of interacting with other subunits of the T-cell they stimulated surface presentation of CD16TM and Jurkat cells expressing the gene were able to initiate the Ca response. Cells expressing the gene for gp120/41 of human immunodeficiency virus were specifically lysed by cells presenting the fusion proteins.

IC ICM A61K037-12
ICS C07K003-00; C07K013-00; C07K015-00; C07K017-00

CC 15-10 (Immunochemistry)

ST T cell receptor **fusion protein** **immunomodulation**; **chimeric** CD4 receptor

IT **Immunomodulators**
(chimeric receptors for, for cell-mediated **immunity**)

IT HeLa cell
Macrophage
Mast cell
Neutrophil
(expression in, of gene for chimeric receptor, modulation of specificity of **immune** response in relation to)

IT **Protein** sequences
(of peptides for **chimeric** receptor construction)

IT Receptors
RL: BIOL (Biological study)
(BCR (B-cell antigen receptors), subunits of, fusion products with ligand-binding domains of, for modulation of **immune** response)

IT Antigens
RL: BIOL (Biological study)
(BCR receptors, subunits of, fusion products with ligand-binding domains of, for modulation of **immune** response)

IT Antigens
RL: BIOL (Biological study)
(CD3, delta, fusion products with ligand-binding domains of, for modulation of **immune** response)

IT Antigens
RL: BIOL (Biological study)
(CD4, chimeric, construction of, **immunomodulation** in relation to)

IT **Immunoglobulins**
RL: BIOL (Biological study)
(G1, fusion products, with **immune** receptors, chimeric gene for, expression in **immune** system cells of, modulation of **immune** response in relation to)

IT Antigens
RL: PRP (Properties)
(MB1, fusion products with ligand-binding domains of, for modulation of **immune** response)

IT **Histocompatibility** antigens
RL: BIOL (Biological study)
(**MHC** (major **histocompatibility** complex), cellular **immune** response mediated through, modulation of, chimeric receptors for)

IT Lymphocyte
(T-cell, expression in, of gene for chimeric receptor, modulation of specificity of **immune** response in relation to)

IT Lymphocyte
(T-cell, cytotoxic, expression in, of gene for chimeric receptor, modulation of specificity of **immune** response in relation to)

IT Antigens
RL: BIOL (Biological study)

(T3, gamma, fusion products with ligand-binding domains of, for modulation of **immune** response)

IT Receptors
RL: BIOL (Biological study)
(TCR (T-cell antigen receptor), subunits of, fusion products with ligand-binding domains of, for modulation of **immune** response)

IT Antigens
RL: BIOL (Biological study)
(TCR receptors, subunits of, fusion products with ligand-binding domains of, for modulation of **immune** response)

IT Gene
RL: BIOL (Biological study)
(**chimeric**, for **fusion proteins** of Igs and **immune** receptors, expression in **immune** system cells of, modulation of **immune** response in relation to)

IT **Proteins**, specific or class
RL: BIOL (Biological study)
(**fusion** products, of Igs and **immune** receptors, **chimeric** gene for, expression in **immune** system cells of, modulation of **immune** response in relation to)

IT **Immunoglobulins**
RL: BIOL (Biological study)
(fusion products, with **immune** receptors, chimeric gene for, expression in **immune** system cells of, modulation of **immune** response in relation to)

IT Leukocyte
(granulocyte, expression in, of gene for chimeric receptor, modulation of specificity of **immune** response in relation to)

IT Lymphocyte
(natural killer cell, expression in, of gene for chimeric receptor, modulation of specificity of **immune** response in relation to)

IT Embryo
(stem cell, expression in, of gene for chimeric receptor, modulation of specificity of **immune** response in relation to)

IT 94717-19-8, Receptor (human T-cell T3 .delta.-subunit precursor **protein** moiety reduced) 104646-02-8, Antigen T 3 (human T-cell clone pJ6T3.gamma. .gamma.-subunit precursor **protein** moiety reduced) 120299-99-2, Glycoprotein (mouse clone pIA94-3 gene B29 precursor **protein** moiety reduced) 121036-15-5, Glycoprotein (mouse clone m-mb-1-W-8 gene mb-1 precursor **protein** moiety reduced) 145385-06-4
RL: PRP (Properties)
(amino acid sequence of, **chimeric** receptor construction in relation to)

IT 141923-04-8 145385-04-2 145385-05-3 146157-54-2, 31-142-Antigen CD 3 (human Jurkat cell .zeta.-chain **protein** moiety) 146157-55-3 146157-56-4 146157-57-5 146157-58-6 146157-59-7 146157-60-0 146157-61-1 146157-62-2 146157-63-3
RL: PRP (Properties)
(amino acid sequence of, **chimeric** receptor contg.)

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=> fil wpids
FILE 'WPIDS' ENTERED AT 12:57:01 ON 04 FEB 2002
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FILE LAST UPDATED: 30 JAN 2002              <20020130/UP>
MOST RECENT DERWENT UPDATE            200207   <200207/DW>
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     (FILE 'WPIDS' ENTERED AT 12:45:11 ON 04 FEB 2002)
               DEL HIS Y
L1         36708 S FUSION OR CHIMER?
L2          4188 S L1 (4A) PROTEIN#
L3          6464 S IG OR IMMUNOGLOBULIN?
L4           512 S L2 AND L3
L5          4015 S MOL? (4A) COMPLEX?
L6          2834 S MULTIVALENT? OR HETERODIMER?
L7          1144 S MHC OR HISTOCOMPATIBIL?
L8           861 S TCR OR T CELL RECEPTOR#
L9            18 S L4 AND  L6
L10           39 S L4 AND (L7 OR L8)
L11            3 S L10 AND L6
L12           16 S L5 AND L4
L13            9 S L12 AND (L6 OR L8 OR L7)
L14           11 S L13 OR L11
L15           99 S L6 (4A) PROTEIN#
L16            0 S L15 AND (L5)
L17            2 S L15 AND (L7 OR L8)
L18           12 S L14 OR L17
L19          158 S LINKER? (4A) PROTEIN#
L20            3 S L10 AND L19
L21           39 S  L4 AND (L7 OR L8)
L22           39 S L21 AND (IMMUN? OR  AUTOIMMUN? )
L23           30 S L21 AND (IMMUNE OR IMMUNITY OR IMMUNOMODU? OR IMMUNOSUPP?)
L24           14 S L20 OR L18
L25           20 S L23 NOT L24

     FILE 'WPIDS' ENTERED AT 12:57:01 ON 04 FEB 2002

=> d .wp tech l24 1-14;d .wp tech l25 1-20

L24  ANSWER 1 OF 14  WPIDS COPYRIGHT 2002   DERWENT INFORMATION LTD
AN   2001-582048 [65]    WPIDS
DNN  N2001-433625        DNC C2001-172567
TI   Phage display library for screening for target molecules, comprises
     recombinant phages containing a vector with a polynucleotide encoding a
```

T-cell receptor recognition element.
DC B04 D16 S03
IN NISSIM, A
PA (NISS-I) NISSIM A
CYC 94
PI WO 2001062908 A2 20010830 (200165)* EN 142p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001032204 A 20010903 (200202)
ADT WO 2001062908 A2 WO 2001-IL120 20010205; AU 2001032204 A AU 2001-32204 20010205
FDT AU 2001032204 A Based on WO 200162908
PRAI US 2000-510361 20000222
AB WO 200162908 A UPAB: 20011108
NOVELTY - A phage-display library (L) for screening for target molecules, comprising recombinant phages each comprising a vector (V) having a polynucleotide (P1) which codes for a **T-cell receptor** (**TCR**) recognition element, and/or a mutation and variant, in which the vector expresses a recombinant **TCR** recognition element from each of the recombinant phages, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a linker which joins the **TCR** recognition element and an **immunoglobulin** (**Ig**) recognition element of a reagent comprising a nucleic acid characterized as:

(i) aiding in folding of the domains; and

(ii) supporting the stabilization of the intact protein construct;

(2) a tag which joins the **TCR** reagent and a **chimeric** reagent with gIII **protein** of the bacteriophage of a reagent comprising a nucleic acid which aids in the purification and detection of the reagent;

(3) a phage displayed recombinant **TCR** recognition element/ **Ig** recognition element reagent;

(4) a soluble reagent detached from phage which includes a recombinant chimeric **TCR** recognition element/**Ig** recognition element reagent;

(5) (V) comprising (P1) and a polynucleotide (P2) which codes for an **Ig** recognition element, and/or a mutation or variant;

(6) an oligonucleotide comprising a nucleic acid sequence, given in the specification;

(7) creating a phage display chimeric **TCR** reagent comprising:

(i) reverse transcribing mRNA of a sample of cells into cDNA of the **TCR** and **Ig**;

(ii) amplifying the cDNA;

(iii) cloning a population of DNA fragments into expression (V);

(iv) combining a genetically diverse repertoire of nucleic acid sequences which each encode a unique or genetically diverse population of a component part of the **TCR**-cell receptor elements to form an (L) of nucleic acid sequences using (V)encoding **TCR**, with the property of specifically binding to a molecule of interest;

(v) expressing (L) from (V) in recombinant host cells, each of the polypeptide chain components being expressed as a recombinant **chimeric protein** on its own or as part of phage particles which are part of (L); and

(vi) selecting from (L), by binding to a molecule of interest, for

example with a MHC-peptide complex, a unique or restricted population of the reagents binding specificity;

(8) a primer comprising a nucleic acid with a sequence given in the specification;

(9) selection against a target molecule comprising:

(a) contacting (L) with the target **molecule** to form a **complex**;

(b) dissociating the bound phage from the complex,

(c) amplifying bound phage by growth in a bacterial host;

(d) repeating the binding, dissociation, and amplification; and

(e) screening the selected library on a target molecule;

(10) diagnosing a subject with a tumor comprising contacting a sample from the subject with (4) which is specific for a specific tumor antigen to form a complex and detecting the complex;

(11) treating a HLA class I associated disease or a pathogenic condition comprising administering (4);

(12) imaging a neoplastic disorder in a subject comprising administering a labeled (4) and detecting the label; and

(13) purifying and detecting (4) of (L), where (4) comprises a linker region or a tag.

ACTIVITY - Antirheumatic; antiarthritic; antiinflammatory; uropathic; opthalmological; antipsoriatic; vasotropic; dermatological; immunosuppressive; antithyroid; thyromimetic; hepatotropic; cytostatic; neuroprotective; nephrotropic. No biological data is given.

MECHANISM OF ACTION - None given.

USE - (L) is used to screen for target molecules. A soluble reagent detached from phage of (L), which includes a recombinant chimeric TCR recognition element/Ig recognition element reagent is used to diagnose a subject with a tumor or image a neoplastic disorder in a subject. It is also used to treat a HLA class I associated disease or a pathogenic condition, such as ankylosing spondylitis, Reiter disease, psoriatic spondylitis; psoriasis vulgaris, Behcet disease, rheumatoid arthritis, pauciarticular juvenile rheumatoid arthritis, systemic lupus erythematosus, sjoegren's disease, IDDM, Addison disease, Graves disease, Hashimoto disease, celiac disease, primary biliary cirrhosis, pemphigus vulgaris, epidermolysis bullosa acquisita, Hodgkin disease, cervical squamous cell carcinoma, multiple sclerosis, optic neuritis, narcolepsi, myasthenia gravis, Goodpasture syndrome or alopecia areata (all claimed). Dwg.0/10

TECH UPTX: 20011108

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Library: (L) further comprises a (P2) and (V) expresses a recombinant chimeric **TCR** recognition element/**Ig** recognition element from each of the recombinant phages. The **TCR** recognition element comprises a variable fragment of the **TCR**, which is **TCR** variable alpha (TCRalpha), TCRbeta, TCRgamma, and/or TCRdelta domains. The **TCR** variable comprises complementary determining residues (CDR) 1, 2, and/or 3. Alternatively the **TCR** recognition element comprises a constant fragment, which is a Calpha, Cbeta1, Cbeta2, Cgamma or Cdelta domain. The **Ig** recognition element is an antibody comprising a variable domain. The antibody comprises a heavy and/or light chain. The chains comprise heavy or light chain variables (VH or VL, respectively). The heavy chain comprises CH1 constant domains and the light chain comprises Ckappa or Cdelta domains. The reagent is a Fv (single chain) or a Fab fragment. (V) comprise a nucleic acid which codes for a second molecule that is linked to the **TCR** and/or the chimeric **TCR/Ig** reagent. The second molecule interacts with a second nonoverlapping determinant of the target molecule or a multimeric target and enhances the overall avidity of the interaction. The **TCR** and/or chimeric **TCR/Ig**

fragment joint to the second molecule is a bispecific molecule. The second molecule is a nucleic acid, DNA, RNA, peptide, polypeptide, enzyme, single chain polypeptide, carbohydrate, glycosphingolipid, fatty acid, organic or inorganic substance, ion, synthetic, or mimetic. The second molecule is a reagent directed against a specific **MHC**/peptide complex coupled to CD8, or variant which exhibits low affinity to their respective target CD8 or anti-beta2m. The phage displayed chimeric **TCR/Ig** fragment is a single chain TCRValpha/VL, TCRVbeta/VL, TCRValpha/VH, TCRVbeta/VH, VL/TCRValpha, VL/TCRVbeta, VH/TCRValpha, VH/TCRVbeta, TCRVgamma/VL, TCRVdelta/VL, TCRVgamma/VH, TCRVdelta/VH, VL/TCRVgamma, VL/TCRVdelta, VH/TCRVgamma, VH/TCRVdelta, TCRValpha/TCRVbeta, TCRValpha/TCRVgamma, TCRValpha/TCRVdelta, TCRVbeta/TCRValpha, TCRVbeta/TCRVgamma, TCRVbeta/TCRVdelta, TCRVgamma/TCRValpha, TCRVgamma/TCRVbeta, TCRVgamma/TCRVdelta, TCRVdelta/TCRValpha, TCRVdelta/TCRVbeta, TCRVdelta/TCRVgamma and/or mutation and variant. The phage displayed recombinant **TCR** fragment is a single chain
Preferred Linker: The nucleic acid in the linker comprises a sequence, given in the specification.
Preferred Reagent: The single chain Fv fragment or Fab fragment is displayed on phage.
Preferred Vector: The polynucleotide encoding the **TCR** and the **immunoglobulin** elements, fragments, domains and/or segments are in a tail-to-head transcriptional orientation. (V) is a plasmid, phage, phagemid, viral vector or a combination. (V) further comprises transcription and translation control sequences.. The transcription control sequence is a promoter, RNA polymerase initiation site, RNA polymerase termination site, TATA box, CAT box, poly A addition site, enhancer or a part or combination of them. The translation control sequence is a ribosome binding site,a leader sequence, or a part or combination of them.
Preferred Method: The method of (9) further comprises characterizing the selected phage. The target and/or (L) are labeled. (L) is attached to a target molecule bound to a support matrix. The support is a plastic dish, virus particle or cell culture. The target molecule comprises cells such as tumor cells, viral infected cells, or cells originated from tissue or organs.

L24 ANSWER 2 OF 14 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2001-514837 [56] WPIDS
DNN N2001-381340 DNC C2001-153938
TI An isolated DNA encoding a hB7-H2 polypeptide, useful for treating cancer, AIDS, or autoimmune diseases (e.g. rheumatoid arthritis, multiple sclerosis or insulin-dependent diabetes mellitus).
DC B04 D16 S03
IN CHEN, L
PA (MAYO-N) MAYO FOUND MEDICAL EDUCATION RES; (MAYO-N) MAYO FOUND MEDICAL EDUCATION & RES
CYC 95
PI WO 2001064704 A1 20010907 (200156)* EN 48p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001045396 A 20010912 (200204)
ADT WO 2001064704 A1 WO 2001-US6769 20010302; AU 2001045396 A AU 2001-45396 20010302
FDT AU 2001045396 A Based on WO 200164704

PRAI US 2000-186519P 20000302
AB WO 200164704 A UPAB: 20011001
NOVELTY - An isolated DNA (N1) encoding a hB7-H2 polypeptide is new.
DETAILED DESCRIPTION - An isolated DNA (N1) encoding a hB7-H2 polypeptide is new.
N1 comprises:
(a) a nucleic acid sequence that encodes a hB7-H2 polypeptide with the ability to co-stimulate a T cell, where the polypeptide is less than 555 amino acids in length and the nucleic acid sequence hybridizes under highly stringent conditions to the complement of a sequence that encodes a polypeptide with the 302 amino acid sequence (I) defined in the specification; or
(b) the complement of the sequence of (a).
INDEPENDENT CLAIMS are included for the following:
(1) an isolated polypeptide (P1) encoded by N1;
(2) a vector comprising N1;
(3) a cell comprising the vector of (2);
(4) a method (M1) of co-stimulating of a T cell, comprising contacting the T cell with P1;
(5) a method (M2) of identifying a compound that inhibits an immune response, comprising providing a test compound, culturing, together, the compound, P1, a T cell, and a T cell activating stimulus, and determining whether the test compound inhibits the response of the T cell to the stimulus, as an indication that the test compound inhibits an immune response;
(6) a method (M3) of identifying a compound that enhances an immune response, comprising providing a test compound, culturing, together, the compound, P1, a T cell, and a T cell activating stimulus, and determining whether the test compound enhances the response of the T cell to the antigen, as an indication that the test compound enhances an immune response;
(7) an antibody that binds specifically to P1;
(8) a cell comprising the vector of (2);
(9) a method of producing a polypeptide that co-stimulates a T cell, comprising culturing the cell of (8) and purifying the polypeptide from the culture;
(10) a **fusion protein** (P2) comprising a first domain joined to at least one additional domain, where the first domain comprises P1;
(11) a nucleic acid molecule (N2) encoding P2;
(12) a vector comprising N2;
(13) a cell comprising the vector of (12); and
(14) a method of producing P2, comprising culturing the cell of (13) and purifying P2 from the culture.
ACTIVITY - Cytostatic; anti-HIV; immunostimulant; antiinflammatory; immunosuppressive; antirheumatic; aniarthritic; antidiabetic.
No biological data given.
MECHANISM OF ACTION - The hB7-H2 polypeptide co-stimulates a T cell.
No biological data given.
USE - The hB7-H2 proteins and its variants are generally useful as immune response-stimulating therapeutics. For example, the polypeptides can be used for treatment of disease conditions characterized by immunosuppression, e.g., cancer, AIDS or AIDS-related complex, other virally or environmentally-induced conditions, and certain congenital immune deficiencies.
They may also be employed to increase immune function that has been impaired by the use of radiotherapy or immunosuppressive drugs such as certain chemotherapeutic agents, and therefore are particularly useful when given in conjunction with such drugs or radiotherapy.
The hB7-H2 nucleic acid and polypeptide can be used to treat

conditions involving cellular immune responses, e.g., inflammatory conditions (such as, for example, those induced by infectious agents including Mycobacterium tuberculosis or M. leprae), or other pathologic cell-mediated responses such as those involved in autoimmune diseases (e.g. rheumatoid arthritis), multiple sclerosis, or insulin-dependent diabetes mellitus).
Dwg.0/7

TECH UPTX: 20011001
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred DNA: N1 encodes a polypeptide comprising the sequence of (I). N1 has the nucleotide sequence defined in the specification.
Preferred Polypeptide: If the hB7-H2 polypeptide sequence is aligned with the sequence of (I), includes a first amino acid residue at a position equivalent to position 301 of wild-type (I), the first amino acid residue is histidine or its conservative substitution.
If the hB7-H2 polypeptide sequence is aligned with the sequence of (I), includes a second amino acid residue at a position equivalent to position 302 of wild-type (I), the first amino acid residue is valine or its conservative substitution.
P1 comprises residues 22-302 or 1-302 of (I), or the amino acid sequence of (I) but differing solely by conservative substitutions.
In the P2, at least one additional domain comprises the constant region of an **immunoglobulin** heavy chain or its fragment.
Preferred Vector: The nucleic acid sequence is operably linked to a regulatory element which allows expression of the nucleic acid sequence in a cell.
Preferred Method: In M2, the stimulus is an antibody that binds to a **T cell receptor** or a CD3 polypeptide. The stimulus is an alloantigen or an antigenic peptide bound to a major **histocompatibility complex** (**MHC**) **molecule** on the surface of an antigen presenting cell (APC). The APC is transfected or transformed with a nucleic acid encoding the polypeptide and the polypeptide is expressed on the surface of the APC.
In M3, the stimulus is an antibody that binds to a **T cell receptor** or a CD3 polypeptide. The stimulus is an alloantigen or an antigenic peptide bound to a **MHC** molecule on the surface of an APC. The APC is transfected or transformed with a nucleic acid encoding the polypeptide and the polypeptide is expressed on the surface of the APC.
Preferred Antibody: The antibody is a monoclonal antibody. The antibody binds to the polypeptide with the sequence of (I).

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: In M1, the contacting comprises culturing the polypeptide with the T cell in vitro. The T cell is in a mammal. The contacting comprises administering the polypeptide to the mammal. The contacting comprises administering a nucleic acid encoding the polypeptide to the mammal. M1 comprises providing a recombinant cell which is the progeny of a cell obtained from the mammal and has been transfected or transformed ex vivo with a nucleic acid encoding the polypeptide so that the cell expresses the polypeptide and administering the cell to the mammal. The cell is an antigen presenting cell (APC) and the cell expresses the polypeptide on its surface. Prior to the administering, the APC is pulsed with an antigen or an antigenic peptide. The mammal is suspected of having an immunodeficiency disease, an inflammatory condition, or an autoimmune disease.

L24 ANSWER 3 OF 14 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2001-397926 [42] WPIDS
DNC C2001-120942

TI Novel DNA encoding immunoregulatory molecule B7-H1, is useful for co-stimulating a T cell for augmenting immunoregulation and for controlling pathologic cell mediated conditions.
DC B04 D16
IN CHEN, L
PA (MAYO-N) MAYO FOUND MEDICAL EDUCATION & RES
CYC 86
PI WO 2001039722 A2 20010607 (200142)* EN 85p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 2001020530 A 20010612 (200154)
ADT WO 2001039722 A2 WO 2000-US32583 20001130; AU 2001020530 A AU 2001-20530 20001130
FDT AU 2001020530 A Based on WO 200139722
PRAI US 2000-649108 20000828; US 1999-451291 19991130
AB WO 200139722 A UPAB: 20010726
NOVELTY - An isolated B7-H1 DNA (I) comprising a sequence encoding B7-H1 polypeptide capable of co-stimulating a T-cell and comprising a sequence (S1) of 290 amino acids fully defined in the specification, where the nucleic acid sequence hybridizes to the complement of the sequence encoding the polypeptide comprising (S1), or its complement, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated B7-H1 polypeptide (II) encoded by (I);
(2) a vector (III) comprising (I);
(3) a cell (IV) comprising (III);
(4) identifying a compound that inhibits an immune response, by providing a test compound, culturing together, the compound with (II), a T cell and a T cell activating stimulus, and determining whether the test compound inhibits the response of the T cell to the stimulus or antigen, as an indication that the test compound inhibits an immune response;
(5) identifying a compound that enhances an immune response, by providing a test compound, culturing, together the compound with (II), a T cell and a T cell activating stimulus and determining whether the test compound enhances the response of the T cell to the stimulus or antigen, as an indication that the test compound enhances an immune response;
(6) an antibody (Ab) that binds specifically to (II);
(7) producing (II);
(8) a **fusion protein** (V) comprising a first domain joined to at least one additional domain, where the first domain comprises (II);
(9) a nucleic acid molecule (VI) encoding (V);
(10) a vector (IIIa) comprising (VI);
(11) a cell (IVa) comprising (IIIa); and
(12) producing (V).

ACTIVITY - Antiinflammatory; immunosuppressive; immunostimulatory. No supporting data given.

MECHANISM OF ACTION - T-cell response co-stimulator (claimed); gene therapy.

To assess whether hB7-H1 co-stimulates T-cell growth, T cells purified from peripheral blood mononuclear cells (PBMC) of healthy human donors were stimulated with hB7-H1Ig in the presence of suboptimal doses of monoclonal antibody (MAb) specific for human CD3. T cell proliferation in 3 day cultures was determined by incorporation of (3H)-thymidine. hB7-H1Ig immobilized on culture plates enhanced T cell proliferation upto 10-fold compared to the control **Ig** in the presence of 5-20 ng/ml

of MAb specific for human CD3, also immobilized on the culture plates. In the absence of MAb specific for human CD3, hB7-H1Ig at a concentration upto 5 micro g/ml induced no T cell proliferation.

USE - (II) is useful for co-stimulating a T-cell such as helper T cell that provides helper activity for a B cell antibody-producing response e.g., IgG2a antibody response, in a mammal having an immunodeficiency disease, inflammatory condition or an autoimmune disease, by culturing (II) with the mammalian T cell in vitro, or administering (II) or (I) to the T-cell, such that the level of CD40 ligand on the T cell surface is increased. The method further involves providing a recombinant cell e.g., an antigen presenting cell (APC) which is the progeny of a cell obtained from the mammal and has been transfected or transformed ex vivo with (I), so that the cell expresses (II), and administering the cell to the mammal. Prior to administration, the APC is pulsed with an antigen or an antigenic peptide (claimed).

Dwg.0/23

TECH UPTX: 20010726

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (II) is produced by culturing (IV) and purifying (II) from the culture. (V) is produced by culturing (IVa) and purifying (V) from the culture (claimed).

Preferred Sequence: (II) comprises a sequence of amino acid residues 23-290 of S1, but differing solely by conservative substitutions. (I) is operably linked to a regulatory element which allows expression of (I) in a cell. Preferred Method: The T-cell activating stimulus is an antibody that binds to a **T-cell receptor** or a CD3 polypeptide, an alloantigen or an antigenic peptide bound to a major **histocompatibility complex** (**MHC**) **molecule** on the surface of an antigen presenting cell (APC). The APC is transfected or transformed with a nucleic acid encoding the polypeptide which is expressed on the surface of the APC. Ab is a monoclonal antibody and binds to (II). At least one additional domain of (V) comprises the constant region of an **immunoglobulin** heavy chain or its fragment.

L24 ANSWER 4 OF 14 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2000-022812 [02] WPIDS
CR 1999-105193 [09]
DNC C2000-005464
TI Peptide linkers, linked fusion polypeptides containing the linkers and their preparation.
DC B04 D16
IN FILPULA, D R; WHITLOW, M D
PA (ENZO-N) ENZON INC
CYC 1
PI US 5990275 A 19991123 (200002)* 42p
ADT US 5990275 A CIP of US 1992-980529 19921120, CIP of US 1993-2845 19930115, Div ex US 1994-224591 19940407, US 1997-926789 19970910
PRAI US 1994-224591 19940407; US 1992-980529 19921120; US 1993-2845 19930115; US 1997-926789 19970910
AB US 5990275 A UPAB: 20000112

NOVELTY - A peptide linker 18-50 amino acids long comprising amino acid sequence (I) is new.

DETAILED DESCRIPTION - (I) has amino acid sequence GSTSGSGXPGSGEGSTKG where X is a charged amino acid, preferably lysine or arginine.

INDEPENDENT CLAIMS are also included for:

(1) a peptide linker 18-50 amino acids long comprising amino acid sequence GSTSGSGKPGSGEGSTKG (II);

(2) a peptide linker 12-50 amino acids long comprising amino acid sequence GSTSGKPSEGKG (III);

(3) a peptide linker 12-50 amino acids long comprising amino acid

sequence GSTSGXPSEGKG (IV) where X is a charged amino acid, preferably lysine or arginine;

(4) a linked fusion polypeptide (A) comprising a first and second polypeptide connected by a peptide linker containing sequence (I), (II), (III) or (IV) positioned to inhibit proteolysis of the linker by subtilisin or trypsin;

(5) a method of preparing (A) from a multi-chain protein comprising:

(a) providing a first polypeptide corresponding to a first chain or subfragment and a second polypeptide corresponding to a second chain or subfragment of the multi-chain protein;

(b) connecting the first and second polypeptides to opposite ends of a peptide linker to form the linked fusion polypeptide, the linker contains sequence (I), (II), (III) or (IV) positioned within the linker sequence to inhibit it's proteolysis by either subtilisin or trypsin; and

(c) recovering (A); and

(6) a method of preparing (A) from two different proteins comprising:

(a) providing a first polypeptide corresponding to a single chain protein or a chain of a multi-chain protein or a subfragment;

(b) providing a second polypeptide corresponding to a single chain protein or a chain of a multi-chain protein different from the first polypeptide or a subfragment; and

(c) connecting the polypeptides and recovering (A) as in (5).

USE - The linkers are used for connecting constituent polypeptides to form novel linked fusion polypeptides. Polypeptides derived from any protein can be connected, in particular multichain protein or protein complexes e.g. enzymes, members of the **immunoglobulin** superfamily, hormones, DNA-binding proteins.

ADVANTAGE - The **linker** provides **fusion proteins** which have greater stability and are less susceptible to aggregation.

Dwg.0/14

TECH UPTX: 20000112

TECHNOLOGY FOCUS - BIOLOGY - Preferred Linker Peptide: The length of the linker peptide depends on the nature of the polypeptides to be linked, the activity of the **fusion protein** resulting from the linkage and the length required to allow the resulting polypeptide to fold in a conformation which provides the desired biological activity.

(I) and (II) preferably comprise 18-30 amino acids and contain the sequence XP at positions 8 and 9 from the amino terminus of the linker.

(I) may be 14-30 amino acids long.

(III) and (IV) preferably comprise 12-30 amino acids and contain the sequence XP at positions 6 and 7 from the amino terminus of the linker.

Preferred Fusion Polypeptide: The first and second polypeptides of (A) may be from different proteins which are single chain or multichain proteins or from the same multichain protein which is a member of the **immunoglobulin** superfamily and is a **T cell receptor** or an **immunoglobulin**. The first polypeptide comprises the binding portion of the variable region of the heavy chain of the **immunoglobulin** and the second polypeptide comprises the binding portion of the variable region of the light chain of the **immunoglobulin** or the first polypeptide comprises the binding portion of the variable region of the light chain of the **immunoglobulin** and the second polypeptide comprises the binding portion of the variable region of the heavy chain of the **immunoglobulin**.

(A) is a single chain antibody (sFv) or a mixed sFv.

L24 ANSWER 5 OF 14 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1999-540586 [45] WPIDS
DNN N1999-400666 DNC C1999-157881

TI New peptides containing at least one epitope from Tek receptor tyrosine kinase, used in vaccines against cancer.
DC B04 D16 S03
IN DURRANT, L G; HEWETT, P W; RAMAGE, J M; SPENDLOVE, I
PA (CANC-N) CANCER RES CAMPAIGN TECHNOLOGY
CYC 85
PI WO 9943801 A1 19990902 (199945)* EN 56p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9926331 A 19990915 (200004)
EP 1056852 A1 20001206 (200064) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9943801 A1 WO 1999-GB583 19990226; AU 9926331 A AU 1999-26331 19990226; EP 1056852 A1 EP 1999-906368 19990226, WO 1999-GB583 19990226
FDT AU 9926331 A Based on WO 9943801; EP 1056852 A1 Based on WO 9943801
PRAI GB 1998-4121 19980226
AB WO 9943801 A UPAB: 19991103
NOVELTY - Peptide (I):

(a) comprises less than the full-length sequence of Tek (a receptor tyrosine kinase);

(b) consists of one or more Tek epitopes, and

(c) binds to major **histocompatibility complex** (**MHC**) **molecules** to stimulate an immune response.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) polypeptide (II) comprising (I) plus at least one sequence not characteristic of Tek;

(b) antibodies (Ab) that bind to (I) or (II), and their fragments, derivatives, functional equivalents or homologs;

(c) cells cultures that produce Ab or their fragments;

(d) nucleic acid (III) that encodes Ab or its fragments;

(e) recombinant DNA construct or virus vector containing a nucleic acid (IV) that encodes (I) or (II);

(f) host cells able to express (IV);

(g) recombinant production of Ab or their fragments by growing cells of (c);

(h) vaccine for targeting endothelial cells (EC) lining the blood vessels of a tumor comprising (I), (II) or the constructs/vectors of (e); (i) (IV);

(j) recombinant production of (I) or (II) by expressing (IV);

(k) vector containing (IV); and

(l) host cell containing the vector of (k).

ACTIVITY - Anticancer; anti-angiogenic.

MECHANISM OF ACTION - (I) bind to **MHC** and the presence of T cell epitopes stimulates helper cell and/or cytotoxic T cell responses. The immune response is directed against endothelial cells (EC) in the tumor-associated vasculature and includes production of antibodies that bind to the cells, causing coagulation and thrombosis. The peptide that had the highest stabilization ratio on HLA-A2, i.e. LMNQHQDPL, was tested at 20 mg/ml for stimulating proliferation of T cells from peripheral blood mononuclear cells, by measurement of incorporation of tritiated thymidine . For a subject of haplotype HLA-DR 1,4, the highest response was after 9 days and was (in counts/min) 3197 compared with 447 for controls. The peptide ITIGRDFEALMNQHQDPLEV, containing two T-cell epitopes, induced proliferation in all cell donors tested.

USE - (I), and its **fusion proteins** (II), are

used:

(1) to generate antibodies (Ab) reactive with epitopes present in wild-type Tek, and

(2) for prevention and treatment of cancer.

(I) and (II), also recombinant DNA constructs or viral vectors that express them, are useful as anticancer vaccines to target endothelial cells (EC) that line blood vessels of the tumor. Nucleic acid (IV) encoding (I) are used for expression of recombinant (I); as source of probes, and to generate transgenic anmals. Ab are used to isolate or purify (I).

ADVANTAGE - The immune response is targeted to EC lining blood vessels of the tumor (these cells overexpress Tek), so damage to even a few EC will kill many tumor cells. These target cells are accessible to the immune response and problems of antigenic heterogeneity, **MHC** loss and resistance to apoptosis (associated with epithelial cells) are unlikely to occur in normal EC.

Dwg.0/5

TECH UPTX: 19991103

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Peptides: (I) contain 1, 2 or more epitopes of Tek which may be (practically) contiguous, and especially lack regions, native to Tek, between the epitopes. Particularly (I) contains at least one segment within the amino acid (aa) regions 55-90, 163-176, 345-362, 427-442 and/or 530-542 of native Tek (sequence given in the specification) or their functional equivalents in Tek variants. These regions have been identified as potential Tek-specific T-cell epitopes. (I) binds HLA (human leucocyte antigen)-A2 with stabilization ratio 1.3 or more, particularly 2.3, and can stimulate T cell proliferation . (II) are particularly **fusion proteins**.

Preferred Vectors: These are plasmids.

Preparation: (IV) is produced by hybridization of target nucleic acid (optionally amplified by polymerase chain reaction) with a probe, encoding a peptide from one of the specified Tek regions or its complement. Once isolated, (IV) can be expressed in any usual vector/host system or in an in vitro system such as a reticulocyte lysate. Monoclonal Ab produced by usual methods can be subjected to recombinant DNA manipulations to produce other, e.g. chimeric, antibodies, e.g. by genetic mutation of hybridomas, by screening recombinant libraries of **immunoglobulin** variable domains or by grafting non-human complementarity-determining regions (CDR) into a human framework.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Antibodies: Ab are monoclonal and suitable fragments are Fab, Fd, (single-chain) Fv, dAb (consisting of variable heavy domains), isolated CDR or F(ab')2. They are prepared by usual immunization and cell fusion techniques.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) can be produced by usual methods of peptide synthesis.

L24 ANSWER 6 OF 14 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1999-527481 [44] WPIDS
DNN N1999-390696 DNC C1999-154975
TI New HMC Class II binding domain **fusion proteins** and conjugates - used for, e.g. treating allergic and autoimmune diseases or detecting, isolating, activating or killing specific T cells.
DC A89 B04 D16 S03
IN STROMINGER, J L; WUCHERPFENNIG, K W
PA (HARD) HARVARD COLLEGE
CYC 84
PI WO 9942597 A1 19990826 (199944)* EN 112p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
UA UG UZ VN YU ZW
AU 9927748 A 19990906 (200003)
BR 9908082 A 20001031 (200060)
EP 1054984 A1 20001129 (200063) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9942597 A1 WO 1999-US3603 19990219; AU 9927748 A AU 1999-27748 19990219; BR 9908082 A BR 1999-8082 19990219, WO 1999-US3603 19990219; EP 1054984 A1 EP 1999-908272 19990219, WO 1999-US3603 19990219
FDT AU 9927748 A Based on WO 9942597; BR 9908082 A Based on WO 9942597; EP 1054984 A1 Based on WO 9942597
PRAI US 1998-75351P 19980219
AB WO 9942597 A UPAB: 19991103
NOVELTY - New monovalent, **multivalent** and multimeric **MHC** Class II binding domain **fusion proteins** and conjugates are new.
DETAILED DESCRIPTION - A novel Class II Major **Histocompatibility** Complex (**MHC**) **fusion protein** comprises a **fusion** of, toward the N-terminus, at least an **MHC** Class II binding domain of an **MHC** Class II alpha or beta chain and, toward the C-terminus, a dimerization domain.
INDEPENDENT CLAIMS are also included for the following: (1) a Class II **MHC fusion protein** comprising a **heterodimer** of a first polypeptide chain and a second polypeptide chain where: (a) the first polypeptide chain comprises a fusion of, toward the N-terminus, at least an extracellular domain of an **MHC** Class II alpha chain, and, toward the C-terminus, a first dimerization domain; (b) the second polypeptide chain comprises a fusion of, toward the N-terminus, at least an extracellular domain of an **MHC** Class II beta chain, and, toward the C-terminus, a second dimerization domain, and (c) the first dimerization domain and the second dimerization domain associate in solution at physiological conditions to form a **heterodimer** capable of selectively binding an **MHC** binding peptide; (2) a Class II **MHC fusion protein** comprising a **heterodimer** of a first polypeptide chain and a second polypeptide chain where: (a) the first polypeptide chain comprises a fusion of, toward the N-terminus, at least an extracellular domain of an **MHC** Class II alpha chain, and toward the C-terminus, an **immunoglobulin** heavy chain C(H)1 constant region; (b) the second polypeptide chain comprises a fusion of, toward the N-terminus, at least an extracellular domain of an **MHC** Class II beta chain and, toward the C-terminus, an **immunoglobulin** light chain constant region; and (c) the **immunoglobulin** heavy chain C(H)1 constant region and the **immunoglobulin** light chain constant region dimerize in solution at physiological conditions to form a **heterodimer** capable of selectively binding an **MHC** binding peptide; (3) a Class II **MHC fusion protein** comprising a **heterodimer** of a first polypeptide chain and a second polypeptide chain, where: (a) the first polypeptide chain comprises a fusion of, toward the N-terminus, at least an extracellular domain of an **MHC** Class II alpha chain and, toward the C-terminus, an **immunoglobulin** light chain constant region; (b) the second polypeptide chain comprises a fusion of, toward the N-terminus, at least an extracellular domain of an **MHC** Class II beta chain and, toward the C-terminus, an **immunoglobulin** heavy chain C(H)1 constant region; and (c) the **immunoglobulin** heavy chain C(H)1 constant region and the **immunoglobulin** light chain

constant region dimerize in solution at physiological conditions to form a **heterodimer** capable of selectively binding an **MHC** binding peptide, and (4) a multimeric **MHC** binding conjugate comprising a carrier and a multiplicity of conjugated **MHC** binding domains.

USE - The **MHC fusion proteins** and conjugates can be used for detecting and isolating T cells having a defined **MHC**/peptide complex specificity (claimed). They can also be used for conferring to a subject adoptive immunity to a defined **MHC**/peptide complex (claimed). They can also be used for stimulating or activating T cells reactive to a defined **MHC** /peptide complex (claimed). They can also be used for selectively killing T cells reactive to a defined **MHC** complex (claimed). They can also be used for tolerizing a subject to a defined **MHC**/peptide complex (claimed). The products can be used for the treatment of allergic and autoimmune diseases, e.g. multiple sclerosis, rheumatoid arthritic, pemphigus vulgaris, and systemic lupus erythematosus. They can also be used for preventing organ or tissue transplant rejection.

ADVANTAGE - None given.

Dwg.0/10

L24 ANSWER 7 OF 14 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1999-418411 [35] WPIDS
DNC C1999-122904
TI Single chain major **histocompatibility** complex class I complexes.
DC B04 D16
IN ACEVEDO, J; BURKHARDT, M; JIAO, J; RHODE, P R; WONG, H C
PA (SUNO-N) SUNOL MOLECULAR CORP
CYC 83
PI WO 9921572 A1 19990506 (199935)* EN 148p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
AU 9898001 A 19990517 (199939)
EP 1027066 A1 20000816 (200040) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CN 1278183 A 20001227 (200123)
US 6232445 B1 20010515 (200129)
KR 2001031205 A 20010416 (200163)
ADT WO 9921572 A1 WO 1998-US21520 19981013; AU 9898001 A AU 1998-98001 19981013; EP 1027066 A1 EP 1998-952256 19981013, WO 1998-US21520 19981013; CN 1278183 A CN 1998-810746 19981013; US 6232445 B1 US 1997-960190 19971029; KR 2001031205 A KR 2000-704156 20000418
FDT AU 9898001 A Based on WO 9921572; EP 1027066 A1 Based on WO 9921572
PRAI US 1997-960190 19971029
AB WO 9921572 A UPAB: 19990902
NOVELTY - New single chain major **histocompatibility** complex (sc-**MHC**) class II complexes comprise a peptide binding groove, and a modified class II beta 2 chain or covalently linked **immunoglobulin** (**Ig**) light chain constant (C1) region.

DETAILED DESCRIPTION - An empty sc-**MHC** class II molecule comprising a peptide binding groove and:

(a) a class II beta 2 chain comprising at least one amino acid substitution or deletion; or

(b) covalently linked IgC1 region or fragment.

INDEPENDENT CLAIMS are also included for the following:

(1) an empty sc-**MHC** class II fusion comprising a peptide

binding groove, where the molecule comprises covalently linked in sequence:

(a) an **MHC** class II beta 1 chain or presenting peptide binding portion;

(b) a modified class II beta 2 chain;

(c) a peptide linker sequence; and

(d) an **MHC** class II alpha 1 alpha 2 chain or presenting peptide binding portion;

(2) an empty sc-**MHC** class II fusion comprising a peptide binding groove, where the molecule comprises covalently linked in sequence:

(a) an **MHC** class II beta 1 beta 2 chain or presenting peptide binding portion;

(b) a peptide linker sequence;

(c) an **MHC** class II alpha 1 alpha 2 chain or presenting peptide binding portion; and

(d) an IgC1 region fragment;

(3) sc-**MHC** class II **fusion proteins** comprising a recombinantly fused presenting peptide and;

(a) a class II beta 2 chain; or

(b) covalently linked IgC1 region or fragment;

(4) sc-**MHC** class II **fusion proteins** comprising a peptide-binding groove, the sc-**MHC** class II fusion molecule comprising covalently linked in sequence a presenting peptide and an empty sc-**MHC** as in (1) or (2);

(5) an empty polyspecific **MHC** complex or fusion comprising a sc-**MHC** class following the general formula (I);

(6) a polyspecific **MHC** complex or fusion comprising an empty sc-**MHC** class II molecule comprising a peptide binding groove, the complex being represented by the formulae A-B-C, B-A-C or A-C-B , provided that when the complex is A-C-B, -C- is not -H;

(7) loaded sc-**MHC** produced by contacting an empty sc-**MHC** or polyspecific **MHC** as above with a presenting peptide under conditions which form a complex between the presenting peptide and the (at least one) empty sc-**MHC**;

(8) a DNA segment encoding the sc-**MHC** class II molecule of (1), (2) or (3);

(9) a DNA segment encoding a portion of a sc-**MHC** class II fusion comprising a peptide-binding groove and an empty sc-**MHC** as in (2), or a polyspecific **MHC** complex as in (6);

(10) DNA vectors comprising DNA as in (8) or (9); and

(11) manufacture of a sc-**MHC** class II **molecule** or polyspecific **MHC complex**.

A = at least one empty sc-**MHC** class II molecule;

B, B1, B2 = are each independently a joining molecule the same or different;

C, C1, C2 = are each independently an effector molecule the same or different; and D = at least one empty sc-**MHC** class II molecule, ligand binding molecule or -H

ACTIVITY - ACTIVITY - Immunosuppressive.

MECHANISM OF ACTION - Vaccine.

USE - The MHC complexes are useful for detection and analysis of peptide ligands, pathogenic T-cells, for functional, cellular and molecular assays. They can be used to identify and/or isolate T cell receptor and/or MHC agonists and antagonists. They can be used in vivo to compete with pathogenic antigen presenting cells involved in immune-related disorders. They can also be used to raise antibodies and to screen immune cells. It is also use in a method of suppressing an immune response in mammals (claimed).

ADVANTAGE - The sc-MHC complexes comprising modified class II beta 2

chains and/or Ig-C1 regions are soluble and provide enhanced yield. These MHC complexes also can contain single antigenic peptides readily isolated from expressing cells in significant quantities. The polyspecific MHC complexes also provide a means to detect cells expressing multiple target structures with a single complex.

DESCRIPTION OF DRAWING(S) - In vivo expression of sc-IAd/OVA suppresses T-cell clonal expansion.

Dwg.8B/8

TECH UPTX: 19990902

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Complexes: The class II beta2 chain is completely deleted, and the sc-**MHC** class II molecule further comprises an IgC1 region fragment.

L24 ANSWER 8 OF 14 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1999-264000 [22] WPIDS
DNC C1999-077902
TI Soluble single-chain **T cell receptor** proteins.
DC B04 D13 D16
IN CARD, K F; WEIDANZ, J A; WONG, H C
PA (SUNO-N) SUNOL MOLECULAR CORP
CYC 82
PI WO 9918129 A1 19990415 (199922)* EN 145p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
AU 9895869 A 19990427 (199936)
EP 1019439 A1 20000719 (200036) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CN 1279690 A 20010110 (200128)
KR 2001030846 A 20010416 (200163)
JP 2001519143 W 20011023 (200202) 161p
ADT WO 9918129 A1 WO 1998-US20263 19980928; AU 9895869 A AU 1998-95869 19980928; EP 1019439 A1 EP 1998-949572 19980928, WO 1998-US20263 19980928; CN 1279690 A CN 1998-811223 19980928; KR 2001030846 A KR 2000-703504 20000331; JP 2001519143 W WO 1998-US20263 19980928, JP 2000-514936 19980928
FDT AU 9895869 A Based on WO 9918129; EP 1019439 A1 Based on WO 9918129; JP 2001519143 W Based on WO 9918129
PRAI US 1997-943086 19971002
AB WO 9918129 A UPAB: 19990609

NOVELTY - A soluble **fusion protein** comprises an **immunoglobulin** (**Ig**) light chain constant region or fragment, covalently linked to a single-chain **T-cell receptor** (sc-**TCR**) comprising a V- alpha chain covalently linked to a V- beta chain by a peptide linker sequence.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a sc-**TCR** produced by contacting a soluble **fusion protein** with an agent capable of cleaving a protein tag;

(2) an sc-**TCR** comprising covalently linked in sequence a V-alpha chain, a C- alpha chain, a peptide linker, a V- beta chain and a C-beta chain;

(3) a DNA segment encoding a sc-**TCR** and comprising a promoter, translation initiation signal and leader sequence in operable linkage;

(4) a DNA vector comprising the DNA segment of (3);

(5) isolating a soluble **fusion protein** and an sc-**TCR** as above;

(6) preparing an antibody capable of specifically binding a **TCR** by administration of a soluble **fusion protein** as above;

(7) and an antibody prepared as in (6).

ACTIVITY - Immunospecific.

MECHANISM OF ACTION - Vaccine.

USE - The soluble **fusion protein** can induce an immune response in a mammal, so that the mammal is immunized against pathogenic **T cell receptor** epitopes (claimed). It can also be used to inhibit T-cell activation in a mammal (claimed). The sc-**TCR** can be used to kill a cell containing a **TCR** specific ligand (claimed). The sc-**TCR** proteins can be used in vitro to detect and analyze ligands such as peptides and **MHC**/HLA molecular components of **TCR** ligands. They can also be used to detect T-cells with pathogenic properties. Other uses include functional, cellular and molecular assays and structural analysis. In vivo the sc-TCRs can compete with pathogenic T cells or to raise antibodies for use in therapy.

ADVANTAGE - Fusion of an **immunoglobulin** (**Ig**) light chain constant region to a single-chain **T-cell receptor** (sc-**TCR**) facilitates soluble expression. The sc-**TCR** can therefore be isolated in significant quantities without performing difficult solubilization, cleaving or re-folding steps. The fusion of the **Ig** light chain to a sc-**TCR** also confers a means of detecting and purifying the **fusion proteins** by conventional immunological methods.

DESCRIPTION OF DRAWING(S) - Diagram showing insert of pNAG1.

Dwg.0/18

TECH UPTX: 19990609

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Fusion Protein**: The sc-**TCR** comprises a V-alpha chain covalently linked at its C-terminus by a peptide linker to the N-terminus of the V-beta chain, or vice versa. The sc-**TCR** additionally comprises a C-beta chain covalently linked between the V-beta C-terminus and the **Ig** light chain, and a C-alpha chain between the V-alpha C-terminus and the peptide linker N-terminus. The **Ig** light chain constant region is a C-kappa chain of 90-110 amino acids in length. The soluble **fusion protein** comprises covalently linked in sequence a V-alpha chain, a peptide linker, a V-beta chain, a C-beta chain and a C-kappa or C-lambda chain or fragment. A C-alpha chain may be linked between the V-alpha chain and the peptide **linker**. A **protein** tag is additionally covalently linked to the soluble **fusion protein**, between the C-beta and C-kappa/C-lambda chains. Alternatively an effector molecule, such as a cell toxin or detectably labeled molecule is covalently linked to the soluble **fusion protein**. The V-alpha and V-beta chains are at least 90% identical to **TCR** V chains present on a cytotoxic T cell. The V or C regions may have been humanized.

L24 ANSWER 9 OF 14 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1999-229248 [19] WPIDS
DNN N1999-169626 DNC C1999-067449
TI **Chimeric protein** of **immunoglobulin** and major **histocompatibility** protein loaded with antigen, used for treating, e.g. autoimmune disease.
DC B04 D16 S03
IN GRETEN, T; O'HERRIN, S M; PARDOLL, D; SCHNECK, J; SLANSKY, J; O'HERRIN, S
PA (UYJO) UNIV JOHNS HOPKINS SCHOOL MEDICINE; (UYJO) UNIV JOHNS HOPKINS

CYC 82
PI WO 9913095 A2 19990318 (199919)* EN 72p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9894776 A 19990329 (199932)
EP 1012320 A2 20000628 (200035) EN
R: AT BE DE DK ES FR GB IE IT NL SE
US 6268411 B1 20010731 (200146)
JP 2001515726 W 20010925 (200170) 96p
ADT WO 9913095 A2 WO 1998-US18909 19980911; AU 9894776 A AU 1998-94776 19980911; EP 1012320 A2 EP 1998-948143 19980911, WO 1998-US18909 19980911; US 6268411 B1 Provisional US 1997-58573P 19970911, Provisional US 1998-82538P 19980421, US 1998-150622 19980910; JP 2001515726 W WO 1998-US18909 19980911, JP 2000-510880 19980911
FDT AU 9894776 A Based on WO 9913095; EP 1012320 A2 Based on WO 9913095; JP 2001515726 W Based on WO 9913095
PRAI US 1998-82538P 19980421; US 1997-58573P 19970911; US 1998-150622 19980910
AB WO 9913095 A UPAB: 19990518
NOVELTY - **Chimeric protein** (I) comprises an **MHC** (major **histocompatibility complex**) **molecule** (II) and an **immunoglobulin** (**Ig**) chain, and exists as a complex of at least two (I). (II) is bound to an antigenic peptide (III), the same for each (II) in the complex.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) vector encoding a (I) in which the **Ig** chain is a heavy chain other than that from IgG1 and is C-terminal to (II);

(2) **chimeric protein** (Ia) comprising (II) and an **Ig** chain that is not IgG heavy chain, existing as a complex of at least two (Ia); and

(3) cells having (I) bound to their surface.

ACTIVITY - Antiviral; antibacterial; antifungal; antitumor; anti-allergy; immunomodulator.

MECHANISM OF ACTION - The complexes interact specifically with antigen-specific T cells to activate or inhibit such cells.

USE - The complexes are used to modulate effector functions of antigen-specific T cells, particularly:

(1) to treat allergy by suppressing an allergy-related T-cell response ((III) is an antigen to which the patient is allergic);

(2) to treat or prevent organ transplant rejection ((III) is an alloantigen);

(3) to treat autoimmune disease ((III) induces an autoimmune response), specifically HTLV(human lymphotropic virus)-1 associated myelopathy/tropical spastic paraparesis (HAM/STP), but many others listed;

(4) to treat tumors by inducing or enhancing an immune response ((III) is a tumor-associated peptide);

(5) to treat an infection by inducing an immune response ((III) is a pathogen-specific peptide), specifically infection by human immune deficiency virus (HIV) or influenza, but more generally any bacterium, virus or fungus; and

(6) to label antigen-specific T cells ((III) binds to these cells), optionally followed by separation and counting of the cells, for diagnosis.

(I) are also used to study **T-cell receptor/MHC** interactions and for lymphocyte tracking.

ADVANTAGE - The complexes are soluble, **multivalent** analogs of **MHC** molecules that bind specifically, with high affinity, to cells bearing (III)-specific receptors (contrast monovalent chimeras that dissociate rapidly). The **Ig** component serves as a scaffold for presentation of the **MHC**-(III) complex and also ensures high stability and easy production as secreted protein. The Fc part of **Ig** may be altered conventionally to impart different biological functions.
Dwg.0/20

TECH UPTX: 19990510
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred complex: (III) is passively or actively bound, particularly to the N-terminus of beta2 macroglobulin or an **MHC** Class II beta-chain, particularly via a peptide tether. Each complex contains two (I) and may be conjugated to a toxin (e.g. ricin) or to a stimulator of the immune response (e.g. a lymphokine) to kill or stimulate target T cells. (II) is an **MHC** Class I molecule, specifically HLA (human leucocyte antigen)2-A2 and (III) is an HTLV (human T-cell lymphotropic virus) Tax11-19 peptide, Gag 77-85 peptide or influenza virus A M158-66 peptide.
Preferred cells: (I) is bound to the surface of dendritic cells, e.g. by expressing (I) that includes a cell-membrane anchor sequence in these cells.
Preparation: An **MHC** gene is linked to the 5'-end of a sequence encoding an **Ig** heavy chain and the recombinant nucleic acid expressed in usual vector/host systems, e.g. insect cells or hybridomas to form (I). These are then loaded with (III) conventionally.

TECHNOLOGY FOCUS - BIOLOGY - To separate antigen-specific T cells, the cells are incubated with (I) containing (II) that binds specifically to such cells. Cells that have bound (III) are then separated, e.g. by flow cytometry and optionally counted. Treatment with (I) may be done in vivo or in vitro and optionally a marker of T cell activation, e.g. a secreted lymphokine, is also detected.

L24 ANSWER 10 OF 14 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1999-180976 [15] WPIDS
DNC C1999-052844
TI Immunologically active molecules - that are epitope-bearing major **histocompatibility** complex class II element/**immunoglobulin** chimeras.
DC B04 D16
IN BONA, C; BRUMEANU, T D; CASARES, S
PA (MOUN) MOUNT SINAI SCHOOL MEDICINE
CYC 22
PI WO 9909064 A1 19990225 (199915)* EN 43p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US
AU 9854285 A 19990308 (199929)
EP 1007567 A1 20000614 (200033) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9909064 A1 WO 1997-US20023 19971104; AU 9854285 A AU 1998-54285 19971104; EP 1007567 A1 EP 1997-948162 19971104, WO 1997-US20023 19971104
FDT AU 9854285 A Based on WO 9909064; EP 1007567 A1 Based on WO 9909064
PRAI US 1997-56185P 19970819
AB WO 9909064 A UPAB: 19990416
NOVELTY - Immunologically active molecules (I) comprising an epitope of interest, more than one major **histocompatibility** complex (**MHC**) class II element, and an **immunoglobulin** constant region, are used to selectively eliminate T lymphocyte cells bearing **T cell receptors** which react with the epitope

of interest.

DETAILED DESCRIPTION - The epitope of (I) is comprised in a **fusion protein** which comprises a **MHC** class II element. Each **MHC** class II element comprises two non- covalently associated chains comprising extracelluar domains of a **MHC** class II protein, and **MHC** class II elements are covalently joined by one or more disulphide linkages present in the **immunoglobulin** (**Ig**) constant region. An INDEPENDENT CLAIM is also included for a method of treating an autoimmune disease or graft versus host disease, comprising administering an effective amount of (I).

USE - The immunologically active molecules of the invention can be used to treat autoimmune diseases or prevent graft versus host disease. Examples of such autoimmune diseases include, but are not limited to, rheumatoid arthritis including juvenile and adult forms, diabetes, multiple sclerosis, systemic lupus erythematosis, scleroderma, sjogren's disease, celiac disease, pemphigus vulgaris, narcolepsy, Grave's disease and Dermatitis Herpetiformis.

ACTIVITY - Antigenic.

MECHANISM OF ACTION - T cell activator.

ADVANTAGE - The molecules of the invention can be used to selectively eliminate T lymphocyte cells bearing **T cell receptors** (TCRs) which react with the epitope of interest in the context of the **MHC** class II element, and so may be used to eliminate or reduce specific T cell populations.

Dwg.0/7

L24 ANSWER 11 OF 14 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1998-159459 [14] WPIDS
DNC C1998-051480
TI New Class II **MHC fusion proteins** - comprising a **MHC** Class II binding domain and a dimerisation domain or an **immunoglobulin** region used for modulating immune responses.
DC B04
IN STROMINGER, J L; WUCHERPFENNIG, K W
PA (HARD) HARVARD COLLEGE
CYC 23
PI WO 9806749 A2 19980219 (199814)* EN 76p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP NZ US
AU 9740723 A 19980306 (199830)
EP 935607 A2 19990818 (199937) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
NZ 333915 A 20001124 (200065)
JP 2000516470 W 20001212 (200101) 91p
AU 730457 B 20010308 (200119)
ADT WO 9806749 A2 WO 1997-US14503 19970815; AU 9740723 A AU 1997-40723 19970815; EP 935607 A2 EP 1997-938386 19970815, WO 1997-US14503 19970815; NZ 333915 A NZ 1997-333915 19970815, WO 1997-US14503 19970815; JP 2000516470 W WO 1997-US14503 19970815, JP 1998-510100 19970815; AU 730457 B AU 1997-40723 19970815
FDT AU 9740723 A Based on WO 9806749; EP 935607 A2 Based on WO 9806749; NZ 333915 A Based on WO 9806749; JP 2000516470 W Based on WO 9806749; AU 730457 B Previous Publ. AU 9740723, Based on WO 9806749
PRAI US 1996-24077P 19960816
AB WO 9806749 A UPAB: 19980406
A Class II Major **Histocompatibility** Complex (**MHC**) **fusion protein** (A) is claimed comprising a fusion of, toward the N-terminus, at least an **MHC** Class II binding domain of an **MHC** Class II alpha or beta chain, and toward the

C-terminus, a dimerisation domain.

Also claimed are: (1) a **heterodimer** made up of two (A), one comprising an extracellular domain of an **MHC** Class II alpha chain and a first dimerisation domain and the other comprising an extracellular domain of an **MHC** Class II beta chain and a second dimerisation domain; the first and second dimerisation domains associate in solution at physiological conditions to form a **heterodimer** capable of selectively binding an **MHC** binding peptide; and (2) an isolated nucleic acid encoding a Class II **MHC fusion protein** (A).

USE - The products can be used for detecting or isolating T cells having a defined Class II **MHC**-peptide complex specificity. They can also be used for tolerising a subject or conferring to a subject adoptive immunity to a defined Class II **MHC**-peptide complex. They can also be used for stimulating or activating cells reactive to a defined Class II **MHC**-peptide complex. They can also be used for selectively killing T cells reactive to a defined Class II **MHC** -peptide complex. In particular the products can be used for the treatment of allergic and autoimmune diseases (e.g. multiple sclerosis (MS), rheumatoid arthritis (RA), pemphigus vulgaris (PV) or systemic lupus erythematosus (SLE)), or for tolerising a subject to foreign tissue before or after organ or tissue transplantation or for vaccination against pathogens.

Dwg.0/7

L24 ANSWER 12 OF 14 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1998-120704 [11] WPIDS
DNC C1998-039744
TI Soluble **fusion protein** of major **histocompatibility** molecule, **linker** and optionally peptide(s) - used to stimulate T cell immunity or inhibit T cell activation specifically according to particular major **histocompatibility** complex-peptide combination.
DC B04
IN CULLEN, C M; HIRSCH, R
PA (CHIL-N) CHILDREN'S HOSPITAL MEDICAL CENT
CYC 22
PI WO 9803552 A2 19980129 (199811)* EN 19p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9736645 A 19980210 (199827)
EP 914347 A2 19990512 (199923) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6197302 B1 20010306 (200115)
US 6211342 B1 20010403 (200120)
ADT WO 9803552 A2 WO 1997-US12324 19970715; AU 9736645 A AU 1997-36645 19970715; EP 914347 A2 EP 1997-933467 19970715, WO 1997-US12324 19970715; US 6197302 B1 Div ex US 1996-683409 19960718, US 1997-914421 19970819; US 6211342 B1 US 1996-683409 19960718
FDT AU 9736645 A Based on WO 9803552; EP 914347 A2 Based on WO 9803552
PRAI US 1996-683409 19960718; US 1997-914421 19970819
AB WO 9803552 A UPAB: 19980316

Fusion protein (I) comprises many **MHC** (major **histocompatibility complex**) **molecules** (II) **complexed** to both a linker (L) and a selected peptide (III) for targeting a **T cell receptor** (**TCR**) and modulating T cell function.

Also claimed are:

(1) **fusion protein** (Ia) comprising many (III) coupled to L, and

(2) **fusion protein** (Ib) comprising two (II) complexed directly to the hinge region of the heavy chain of an **immunoglobulin** (**Ig**).

USE - (Ia) is used to stimulate T cell immunity (when L can deliver a second, activating signal, or to destroy T cells when a toxin or radioisotope is also present), while (I) are used to inhibit T cell activity (provided L can not deliver a second signal). Typical uses of (I) and (Ia) are in treatment of autoimmunity, infections, malignancies and transplant rejection.

Generally 0.001-100 mg **fusion protein**/kg is administered.

ADVANTAGE - The **fusion proteins** are soluble and modulate only those T cells that respond to a specific combination of (II) and (III), i.e. they leave the majority of T cells unaffected, avoiding the problem of generalised T cell suppression.

Dwg.1/2

L24 ANSWER 13 OF 14 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1997-489652 [45] WPIDS
DNN N1997-407821 DNC C1997-156136
TI New soluble recombinant divalent and **multivalent proteins** - used for modulating immune responses for treating e.g. transplant rejection, auto-immune disorders, tumours or viral infection.
DC B04 D16 S03
IN OHERRIN, S; SCHNECK, J P; O'HERRIN, S; SCHNECK, J; HAMAD, A; LEBOWITZ, M S
PA (UYJO) UNIV JOHNS HOPKINS; (UYJO) UNIV JOHNS HOPKINS SCHOOL MEDICINE
CYC 76
PI WO 9735991 A1 19971002 (199745)* EN 80p
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9724224 A 19971017 (199807)
EP 889964 A1 19990113 (199907) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 11507843 W 19990713 (199938) 80p
US 6015884 A 20000118 (200011)
NZ 331688 A 20000228 (200017)
US 6140113 A 20001031 (200057)
KR 2000005060 A 20000125 (200061)
AU 729406 B 20010201 (200112)
ADT WO 9735991 A1 WO 1997-US4694 19970328; AU 9724224 A AU 1997-24224 19970328; EP 889964 A1 EP 1997-919902 19970328, WO 1997-US4694 19970328; JP 11507843 W JP 1997-534519 19970328, WO 1997-US4694 19970328; US 6015884 A Provisional US 1996-14367P 19960328, US 1997-828712 19970328; NZ 331688 A NZ 1997-331688 19970328, WO 1997-US4694 19970328; US 6140113 A Provisional US 1996-14367P 19960328, CIP of US 1997-828712 19970328, US 1998-63276 19980421; KR 2000005060 A WO 1997-US4694 19970328, KR 1998-707687 19980928; AU 729406 B AU 1997-24224 19970328
FDT AU 9724224 A Based on WO 9735991; EP 889964 A1 Based on WO 9735991; JP 11507843 W Based on WO 9735991; NZ 331688 A Based on WO 9735991; US 6140113 A CIP of US 6015884; KR 2000005060 A Based on WO 9735991; AU 729406 B Previous Publ. AU 9724224, Based on WO 9735991
PRAI US 1996-14367P 19960328; US 1997-828712 19970328; US 1998-63276 19980421
AB WO 9735991 A UPAB: 19971113
A soluble recombinant divalent or **multivalent protein** composition comprising the extracellular domains of a **heterodimeric protein** operatively linked to

immunoglobulin heavy and light chain polypeptides is new.

USE - The protein compositions are capable of specifically binding target molecules to regulate immune responses. They can selectively increase or decrease cellular activation, proliferation, anergy, or deletion of specific T cell subsets. They can be used for selectively inhibiting or decreasing an immune response such as a response directed to a foreign transplantation antigen or a response resulting in an autoimmune disease. When the **heterodimeric protein** is a **MHC** class II molecule and further comprises an antigenic peptide, the protein compositions can be used for stimulating an antigen-specific T-cell response. When the **heterodimeric protein** is a **T cell receptor** (**TcR**) molecule, the protein compositions can be used for identifying and purifying an unknown peptide/**MHC** complex which may be involved in cancer or infectious diseases such as AIDS. The compositions can also be used for destroying viral-infected or tumour cells. In particular, the compositions can be used for treating autoimmune diseases, AIDS, Epstein Barr virus associated diseases, virus (AIDS or EBV) associated B cell lymphoma, chronic fatigue syndrome, parasitic diseases and immunosuppressed disease states, such as viral infections following allograft transplantation or AIDS, cancers, chronic active hepatitis, diabetes, toxic shock syndrome, food poisoning, or transplant rejection.

ADVANTAGE The compositions have high affinity for their target molecules. Use of the compositions allows selective immune modulation without compromising the general performance of the immune system.

Dwg.0/13

L24 ANSWER 14 OF 14 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1994-358283 [44] WPIDS
DNC C1994-163544
TI Chimeric cpds. with DNA binding and ligand binding components - forming complexes with DNA for transfer of genes to specific target cells, for gene therapy.
DC B04 D16
IN LEDLEY, F D; STANKOVICS, J
PA (BAYU) BAYLOR COLLEGE MEDICINE
CYC 49
PI WO 9425608 A1 19941110 (199444)* EN 42p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KP KR KZ LK LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SK UA UZ VN
AU 9467138 A 19941121 (199508)
US 6191257 B1 20010220 (200112)
ADT WO 9425608 A1 WO 1994-US4589 19940425; AU 9467138 A AU 1994-67138 19940425; US 6191257 B1 Cont of US 1993-54493 19930427, US 1995-480935 19950607
FDT AU 9467138 A Based on WO 9425608
PRAI US 1993-54493 19930427; US 1995-480935 19950607
AB WO 9425608 A UPAB: 19950619
Chimeric cpd. (A) comprising a DNA-binding element (I) and a ligand-binding element (II) is new. (I) is lactoferrin (Ia),histone, nuclear hormone receptor, transacting regulatory element, basic nuclear protein or chromatin element. (II) is a glycoprotein hormone, serum protein, vitamin binding protein, transcobalmin I or II, R binder, intrinsic factor, cell surface protein, cytokine, neuropeptide, viral or bacterial protein, cell adhesion molecule, **immunoglobulin**, **T-cell receptor**, or cell surface marker from (im)mature bone marrow or lymphocyte. Also new are (1) complexes for gene transfer (B) of DNA (III) bound to (A); (2) **chimeric** recombinant DNA-binding **protein** (A') comprising elements binding to a target

cell receptor and DNA in a single **molecule**; (3) **complexes** (B') of (III) bound to (A'); (4) complex of (Ia) bound to a DNA vector.

USE - The complexes are useful in gene transfer (gene therapy), for expressing a protein, anti-sense nucleic acid or enzymatically active RNA. The complexes can be admin. orally, parenterally, topically or by inhalation (claimed).

ADVANTAGE - The complexes allow specific targetting of DNA; improved uptake in many different cell types and endosomal de-stabilisation without use of viral proteins or chemical/enzymatic modification of DNA or ligand. Gene transfer is easier and safer, compared with current methods.

Dwg.2/10

L25 ANSWER 1 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2001-657582 [76] WPIDS
DNC C2001-193657
TI Gene complex for reversible cell immortalization, useful for expanding cells for cell replacement therapy of e.g. neurodegenerative disease, contains removable immortalizing gene.
DC B04 D16
IN KANDOLF, R; KUEPPER, J; KUHN, A
PA (UYTU-N) UNIV TUEBINGEN EBERHARD-KARLS
CYC 23
PI DE 10019195 A1 20011025 (200176)* 10p
WO 2001078757 A2 20011025 (200176) DE
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU CA JP US
ADT DE 10019195 A1 DE 2000-10019195 20000417; WO 2001078757 A2 WO 2001-EP2967 20010315
PRAI DE 2000-10019195 20000417
AB DE 10019195 A UPAB: 20011227

NOVELTY - Gene complex (A) for reversible immortalization of cells, comprising an immortalizing gene region (B), two flanking sequences (FS) around (B) that function as sites for homologous recombination, and at least one promoter upstream of (B), is new. (B) contains at least one resistance gene (RG), an immortalizing gene (**IG**) and preferably a suicide gene (SG).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) gene complex (A1) for **immunomodulation** of cells comprising first **immunomodulatory** gene region (C1), expression of which inhibits the function of **MHC** (major **histocompatibility** complex) Class I on cells, a second **immunomodulatory** gene region (C2) expression of which inactivates NK (natural killer) cells, and RG;

(2) producing cells (D) by preparing organ-related cells, immortalizing them, expanding and then reversing the immortalization;

(3) cells produced by the method of (2);

(4) pharmaceutical composition containing cells of (3);

(5) plasmid or viral vector that contains (A) or (A1);

(6) transplant material that contains cells of (3); and

(7) kit containing (A) or (A1).

ACTIVITY - Cardiant; antiParkinsonian; osteopathic; hepatotropic; antiinflammatory.

No biological data is given.

MECHANISM OF ACTION - Cell and protein replacement.

USE - (A) is used to immortalize cells so that these can be expanded

in culture and, after reversal of immortalization, used to produce transplants for organ regeneration (for treating myocardial, neurodegenerative, bone and liver diseases, e.g. infarction, Parkinson's disease, osteoporosis or chronic liver inflammation), also for treatment of chronic diseases. The cells may also be used for extracellular preparation of tissues, e.g. seeded into collagen/fibronectin biomaterials to produce e.g. cardiac or venous valves.

ADVANTAGE - The construct provides immunologically and clinically tolerable cells inexpensively and in practically unlimited quantities. Allogenic cells can be rendered immunotolerant by transforming with a modulatory gene construct.

Dwg.0/2

TECH UPTX: 20011227

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Complex: (A) also contains a transformation gene (TG), particularly an oncogene (especially encoding the SV40 tumor antigen) or a telomerase gene.

Preferred Materials: SG is the thymidine kinase gene and FS are loxP sites. In (A1), the first **immunomodulatory** region contains e.g. a cytomegalovirus (CMV), herpes simplex virus, human **immune** deficiency virus or adenovirus gene, e.g. the CMV U52 gene, or a gene that encodes a single-chain antibody (scFv) for blockading **MHC** Class I presentation. The second **immunomodulatory** region contains the CMV UL18 gene or a gene that encodes a recombinant scFv that is anchored to the cell membrane and protects against NK cells.

Preferred Method: In the method of (2), the starting cell is a multipotent stem cell, particularly a mesenchymal stromal cell from bone marrow and expansion of the immortalized cells includes adding at least one factor that stimulates differentiation to organ-specific cells, particularly cardiomyocytes, bone or cartilage cells. Specific differentiation agents are dexamethasone, 5'-azacytidine, trichostatin A, all-trans retinoic acid and amphotericin. Particularly at least 2, preferably 4, differentiation agents are used. Alternatively, the starting cells are resting, terminally differentiated cells and these may be transfected at the same time as they are immortalized. The cells may be autologous or allogenic, and if allogenic, they are rendered immunotolerant by:

(a) transforming with (A1);

(b) treatment with a monoclonal antibody that blocks NK-mediated cell lysis; or

(c) knocking out at least one gene, e.g. for beta2 microglobulin, that blocks **MHC** Class I presentation.

Reversal of immortalization after expansion is particularly by treatment with Cre recombinase, especially where this is provided as a recombinant **fusion protein** or by infection with a recombinant virus that expresses the enzyme. Treated cells are then selected for successful deletion of SG.

L25 ANSWER 2 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2001-441773 [47] WPIDS
DNN N2001-326781 DNC C2001-133513
TI New recombinant **fusion protein**, useful for treating arthritis, asthma, psoriasis, leukemia and sarcoidosis, comprises placental protein 14 polypeptide fused to polypeptide sequence of Fc region of **immunoglobulin** protein.
DC B04 D16 P31
IN RIELY, G J; TYKOCINSKI, M L
PA (TRAS-N) TR ASSOC LLC
CYC 94
PI WO 2001049163 A1 20010712 (200147)* EN 28p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001027558 A 20010716 (200169)

ADT WO 2001049163 A1 WO 2001-US104 20010103; AU 2001027558 A AU 2001-27558 20010103

FDT AU 2001027558 A Based on WO 200149163

PRAI US 2000-174287P 20000103

AB WO 200149163 A UPAB: 20010822

NOVELTY - A recombinant **fusion protein** (I) comprising a first domain containing a placental protein (PP) 14 polypeptide sequence (P1) and a second domain comprising a polypeptide sequence (P2) of the Fc region of an **immunoglobulin** protein, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the preparation of (I).

ACTIVITY - Antiarthritic; antiasthmatic; **immunosuppressive**; antiinflammatory; dermatological; antiallergic; neuroprotective; antipsoriatic; antithyroid; antirheumatic; cytostatic.

MECHANISM OF ACTION - Gene therapy; interleukin 1 production inhibitor; T cell activation inhibitor; desensitizes signaling through **T cell receptor**.

The ability of placental protein (PP) 14-Fc gamma 1 to inhibit T-cell proliferation in the absence of alpha 2-macroglobulin (alpha 2M) was directly tested. Purified human T-cells in serum-free conditions were stimulated with solid-phase anti-CD3 mAb (2 micro g/ml) and soluble anti-CD28 mAb (9.3, final concentration 1 micro g/ml), with(out) 10% fetal bovine serum in the presence of 12.5% amniotic fluid or 12 micro g PP14-Fc gamma 1. Proliferation was assessed. Both native PP14 (in amniotic fluid) and PP14-Fc gamma 1 markedly inhibited T-cell proliferation in the presence of serum. In the absence of serum, however, the immunoinhibitory capacities of PP14 and PP14-Fc gamma 1 diverged. While native PP14's capacity to inhibit T-cell proliferation was dramatically reduced in the absence of serum, PP14-Fc gamma retained its immunoinhibitory potential under serum-free conditions, that is, culture conditions shown which alpha 2M was absent. These data indicated that PP14-Fc gamma 1, unlike native PP14, did not depend upon alpha 2M for its immunoinhibitory function.

USE - (I) or a genetic sequence encoding (I) is useful for treating a **immune** disorder e.g., autoimmune, alloimmune, allergic, inflammatory or lymphoproliferative disorders in a patient. (I) is thus useful for treating disorders such as arthritis, asthma, graft-versus-host disease, organ rejection, systemic lupus erythematosus, atopic allergy, inflammatory bowel disease, multiple sclerosis, systemic sclerosis, allergic dermatitis, psoriasis, autoimmune thyroiditis, autoimmune liver disease, and sarcoidosis, rheumatoid arthritis, a neoplastic disorder such as leukemia. The lymphoproliferative disorders are malignant non-Hodgkin's lymphoma, Hodgkin's disease or malignant histiocytosis. (I) or a genetic sequence encoding (I) is useful for inhibiting interleukin 1 production and a Th1 cytokine response in a patient (claimed).

ADVANTAGE - (I) has less toxicity or produces no significant side effects. Modulation of **T cell receptor** responses that is achieved, commensurating with the need to down regulate the cytokine output that is causing **immune** system to inappropriately attack healthy cells, while in the same time allows the **immune** system to protect individual by retaining a sufficient degree of **immune** protection against infectious agents. The **fusion proteins**, unlike PP14 do not depend on alpha 2-macroglobulin for their immunoinhibitory function.

Dwg.0/5

TECH UPTX: 20010822

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: Preparation of (I) involves linking a first polynucleotide sequence encoding (P1) to a second polynucleotide sequence encoding (P2) to generate a chimeric coding sequence, subcloning the chimeric coding sequence into an expression vector, transfecting a cell with the expression vector and purifying (I) expressed by the transfected cell (claimed).
Preferred **Fusion Protein**: (I) comprises (P1) and a second domain comprising a polypeptide sequence of the Fc region of **immunoglobulin** IgG1 or IgG2a, IgG2b, IgG3, IgG4, IgM, IgA or IgE. Preferably the Fc region is the multi-domain Fc region from a human **immunoglobulin** protein. (I) further comprises an epitope tag e.g., polyhistidine tag or a leucine zipper.
Preferred Method: The expression vector used in preparation of (I) is a viral vector or non-viral vector such as plasmid that comprises Epstein-Barr virus episomal replication elements. Preferably, the expression vector is pREP7beta. The purification of (I) is carried out by protein A or protein G affinity chromatography.

L25 ANSWER 3 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2001-398077 [42] WPIDS
DNC C2001-121057
TI Novel vaccine composition comprising protein L, its analog or fragment, useful for enhancing **immune** response to an antigen in an individual.
DC B04 D16
IN BJORCK, L; LEANDERSON, T; WICK, M J
PA (ACTI-N) ACTINOVA LTD
CYC 94
PI WO 2001043769 A2 20010621 (200142)* EN 25p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001021993 A 20010625 (200162)
ADT WO 2001043769 A2 WO 2000-GB4830 20001215; AU 2001021993 A AU 2001-21993 20001215
FDT AU 2001021993 A Based on WO 200143769
PRAI GB 1999-29937 19991217
AB WO 200143769 A UPAB: 20010726
NOVELTY - A vaccine composition (I) comprising protein L, its analog or fragment, coupled to a heterologous antigen, is new.
ACTIVITY - **Immunosuppressive.**
MECHANISM OF ACTION - Vaccine (claimed). Preparations of Protein L B1-B4, B1-B1 or B1 were incubated with splenocytes from mice for 24, 48 or 72 hours in the presence or absence of 10 micro g/ml PMB. The level of surface expression of the co-stimulatory molecules B7-1, B7-2 and CD40, as well as **MHC**-I and **MHC**-II expression on B cells, was analyzed by fluorescence-activated cell sorting (FACS). The result showed that protein L B1-B4 (5 micro g) as well as B1-B1 (10 micro g) and B1 (10 micro g) caused up regulation of B7-2 expression on gated B220+ cells, with the most dramatic effect occurring with B1-B4. B1-B4 also upregulated CD40 and **MHC**-I expression, but had no apparent effect on **MHC**-II. A slight influence of B1-B1 and B1 on surface expression of CD40 and **MHC**-I was detectable.
USE - (I) is useful for enhancing an **immune** response to an antigen in an individual (claimed). Protein L is useful for treating autoimmune diseases.
Dwg.0/5

TECH UPTX: 20010726
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Composition: (I) comprises a **fusion protein** of (I) and a heterologous antigen. (I) further comprises a single **immunoglobulin** binding domain of protein L. The polypeptide is formulated together with an antigen for co-administration to an individual. (I) further comprises an antigen and protein L, to enhance an **immune** response to the antigen.

L25 ANSWER 4 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2001-374265 [39] WPIDS
DNC C2001-114294
TI Pretreating animal for inducing tolerance to gene transfer products by treating animal with hematopoietic stem cells transduced with vector or polynucleotide, which is to be introduced into animal through gene therapy.
DC B04 D16
IN ANDERSSON, G K
PA (BIOT-N) BIOTRANSPLANT INC
CYC 93
PI WO 2001025398 A2 20010412 (200139)* EN 69p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000077406 A 20010510 (200143)
ADT WO 2001025398 A2 WO 2000-US26946 20000929; AU 2000077406 A AU 2000-77406 20000929
FDT AU 2000077406 A Based on WO 200125398
PRAI US 1999-157233P 19991001
AB WO 200125398 A UPAB: 20010716
NOVELTY - Pretreating an animal that is to receive one of a vector (I) encoding a therapeutic polypeptide or recombinant cells comprising (I) or a polynucleotide (II) encoding the therapeutic polypeptide involves treating the animal with hematopoietic stem cells (HSC) transduced with (I) or (II).

ACTIVITY - Antianemic; immunostimulant; hemostatic; antilipemic; **immunosuppressive**; cytostatic.

MECHANISM OF ACTION - Gene therapy. No supporting data is given.

USE - Pretreating an animal that is to receive one of (I) encoding a therapeutic polypeptide to alleviate a genetic deficiency disease or recombinant cells comprising (I) or a (II) encoding the therapeutic polypeptide. The genetic deficiency disease which is alleviated by the gene product encoded by (I) is cystic fibrosis, muscular dystrophy, hemophilia A, hemophilia B, familial hypercholesterolemia, hemoglobinopathies, thalassemia, sickle cell anemia, Gaucher's disease, alpha 1-antitrypsin deficiency, inherited emphysema, chronic granulomatous disease, Fanconi's anemia, and immunodeficiency disease. The therapeutic gene product also acts to reduce a detrimental **immune** response such as an autoimmune disease or an atopic disease. Also the therapeutic gene acts to alleviate or prevent cancer in a patient afflicted with or is at risk for developing cancer. In this case the pretreatment method involves introducing into the animal, a vector (e.g. adenoviral or retroviral vector) that transduces cancer cells and which contains a gene (Herpes simplex virus thymidine kinase (HSV-TK) whose gene product will sensitize the cancer cells to one or more cytotoxic agents e.g. gancyclovir (claimed). The method is useful for alleviating or ameliorating adverse **immune** response and inducing immunological tolerance in an animal receiving genetically different cells or gene

therapy vectors. The method inhibits adverse **immune** responses to transplantation through transplantation of organs or as a result of gene therapy. The methods develop immunological tolerance in gene therapy, utilizing the host's ability to mount an **immune** response against neoantigens in a beneficial manner.

ADVANTAGE - The methods are suitable for inducing immunological tolerance in an animal. Severe problems associated with **immune** responses directed against transgene encoded proteins are effectively eliminated by this method.

Dwg.0/1

TECH UPTX: 20010716

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The pretreatment is preceded by a myeloreductive treatment which involves treating the patient with an **immunosuppressive** regimen to prevent rejection of transduced HSC. The method further involves treating the animal with an **immunosuppressive** regimen separate from the above mentioned one to prevent a graft versus host rejection mediated by the stem cells. The **immunosuppressive** regimen comprises a treatment that inactivates and/or depletes host T lymphocytes and/or natural killer cells (NK) of the patient. Alternately, the **immunosuppressive** regimen involves treatment with T cell depleting anti-CD4 antibodies, CD8 antibodies or more. Preferably, the antibodies are anti-thymocyte globulin (ATG), OKT3 monoclonal antibody, MEDI-507 monoclonal antibody, or humanized-LO-CD2a antibody. The **immunosuppressive** regimen is also carried out by thymic irradiation, sub-lethal whole body irradiation, or both. The **immunosuppressive** regimen is also performed by treating with an **immunosuppressive** agent such as a macrolide **immunosuppressant**, azathioprine, steroids (e.g. prednisone and methyl prednisolone), co-stimulatory (e.g. anti-CD40 ligand antibody or CTLA 4-**Ig fusion protein**) blocking agents, or any of the above mentioned compounds in equal or different relative dosages. The myeloreductive treatment also involves treatment with a cytoreductive agent such as cyclophosphoamide, and treatment with both thymic irradiation and T cell inactivating antibodies such as humanized-LO-CD2a antibody. Preferably, in the pretreatment method the hematopoietic stem cells which are administered are CD34+ cells and are allogenic stem cells, autologous stem cells, syngeneic stem cells, or xenogenic stem cells such as swine stem cells which are from a miniature swine that has been inbred at the swine major **histocompatibility** complex (**MHC**). Alternately, HSC which is administered are bone marrow cells, mobilized peripheral blood cells, cord blood cells or pluripotent stem cells. The pretreatment is carried out in a human being with HSC derived from same human being. In all the above mentioned cases the HSC and the somatic cells are preferably derived from the same animal.

L25 ANSWER 5 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2001-281836 [29] WPIDS
DNC C2001-085769
TI Antigen-specific modulation of **immune** responses, useful for treating or preventing graft rejection, using specific regulatory T cells or their inhibitors.
DC B04 D16
IN YOUNG, K; ZHANG, L; ZHANG, Z X; YANG, L
PA (YOUN-I) YOUNG K; (ZHAN-I) ZHANG L; (ZHAN-I) ZHANG Z X; (YANG-I) YANG L
CYC 94
PI WO 2001026679 A2 20010419 (200129)* EN 73p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC

LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

CA 2316089 A1 20010408 (200131) EN

AU 2000076369 A 20010423 (200147)

ADT WO 2001026679 A2 WO 2000-CA1172 20001006; CA 2316089 A1 CA 2000-2316089 20000824; AU 2000076369 A AU 2000-76369 20001006

FDT AU 2000076369 A Based on WO 200126679

PRAI US 2000-226573P 20000821; US 1999-158132P 19991008

AB WO 200126679 A UPAB: 20010528

NOVELTY - Use, for suppressing an **immune** response, of

(i) regulatory T cells (A) having the phenotype CD3+ alpha beta **TCR**+CD4-CD8-CD11a+CD18+CD25+CD28+CD44-NK1.1- Ly-6A+;

(ii) an agent (I) that stimulates (A);

(iii) a Ly-6A protein (II), or nucleic acid encoding it; or

(iv) an osteopontin protein (III), or nucleic acid encoding it.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) use of an agent (IV) that inhibits (A), Ly-6A or osteopontin for enhancing an **immune** response;

(2) method for in vitro expansion of (A);

(3) isolated (A); and

(4) antibodies (Ab) that bind to (A).

ACTIVITY - **Immunosuppressant; immunomodulatory;** antidiabetic; anti-inflammatory; anti-allergic; antirejection; antimicrobial.

MECHANISM OF ACTION - Suppression or activation of a cytotoxic T cell (CTL) response in an antigen-specific manner, including induction of antigen-specific tolerance. Probably, since (A) express Fas ligand at high levels, they capture alloantigens from antigen-presenting cells (through the anti-host **T cell receptor**), turning them into killer cells. These cells, with captured antigens on their surfaces, attract activated anti-host CTL and send death signals to them through Fas ligand. The process depends on Fas/Fas ligand contact so (A) will not cause guest versus host disease themselves since most host tissues, although expressing Class I **MHC**, do not express Fas.

USE - The method is used, in human or veterinary medicine:

(a) to treat or prevent graft rejection (particularly of skin or heart); guest versus host disease; a wide range of autoimmune diseases (e.g. multiple sclerosis, rheumatism, diabetes etc.) or allergies; or

(b) when used to promote an **immune** response, to treat infections and acquired **immune** deficiency syndrome.

Antibody (Ab) that bind to (A) can be used to suppress or enhance an **immune** response; to isolate or purify (A), and for identifying proteins important for survival and function of (A). When B6xC.B-17 mice were injected intravenously with 30 million viable spleen cells from 2 x dm2 mice (i.e. a mismatch at only one Class I locus Ld), none of them developed guest versus host disease (GVHD) and all survived at least 150 days. When the animals were injected similarly with fully mismatched cells from B6 mice, they all developed severe GVHD and were dead within 2 weeks.

Dwg.0/16

TECH UPTX: 20010528

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: When used to prevent rejection of heart transplants, the treatment composition also contains antibodies to CD4. Preferred Materials: (II) and (III) are soluble **fusion proteins**, with an **immunoglobulin** Fc region, and (I) is an antibody or antigen. (IV) inhibits (A) is an antibody, cyclosporin A, interleukin (IL)-10, anti-interferon-gamma antibody, anti-**TCR** (**T-cell receptor**) antibody, or an agent (specifically soluble Fas) that inhibits interaction between Fas ligand and Fas on a

target cell. (IV) that inhibits Ly-6A or osteopontin is particularly an antibody or antisense oligonucleotide.
TECHNOLOGY FOCUS - BIOLOGY - Process: In method (2), a sample containing regulatory T cells or their precursors (especially from blood or bone marrow) is stimulated with an antigen (any, depending on the required specificity of (A)), then cultured under conditions that cause expansion of (A), particularly presence of IL-2, and preferably also IL-4.
The antigen is particularly:
(a) an allogenic lymphocyte, mismatched at one **MHC** (major **histocompatibility** complex) Class I locus;
(b) an autoantigen; or
(c) an allergen.
Especially the sample is depleted of CD4+ and CD8+ cells before stimulation.
Preferred Cells: (A) express Ly-6A and osteopontin; they do not express IL-2, -4, -10 or -13, but after activation do express mRNAs for interferon-gamma, tumor necrosis factor-alpha and transforming growth factor-beta. They are resistant to activation-induced death but become susceptible to apoptosis in presence of IL-10 and/or antibodies that bind to them. Preparation: Ab are produced by conventional immunization with (A).

L25 ANSWER 6 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2001-007312 [01] WPIDS
DNN N2001-005237 DNC C2001-001874
TI Novel vector expressing secreted antigen fused to cell binding element, useful in vaccines for treatment of e.g. cancer and infection, also identification of epitopes.
DC B04 D16 S03
IN CHEN, S; YOU, Z
PA (UYWA-N) UNIV WAKE FOREST
CYC 92
PI WO 2000067761 A1 20001116 (200101)* EN 163p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000047001 A 20001121 (200112)
ADT WO 2000067761 A1 WO 2000-US12177 20000505; AU 2000047001 A AU 2000-47001 20000505
FDT AU 2000047001 A Based on WO 200067761
PRAI US 1999-132752P 19990506; US 1999-132750P 19990506
AB WO 200067761 A UPAB: 20001230
NOVELTY - Expression vector (A) comprising a promoter (P), sequences encoding a signal sequence (SS), an antigen (Ag) and a cell-binding element (CBE), and a polyadenylation sequence, all operably linked, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(a) transformed cell containing (A);
(b) **fusion protein** (FP) of SS, Ag and CBE;
(c) vaccine comprising (A), antigen-presenting cell (APC) transduced in vitro with FP or with (A), or FP;
(d) expression vector (A') comprising at least sequences encoding SS, Ag and CBE;
(e) identifying a polynucleotide (I) that encodes at least one **MHC** (major **histocompatibility** complex)-II-restricted epitope able to activate CD4+ helper cells or to elicit an **immune**

response in vivo;
(f) producing the vaccines;
(g) simultaneous induction of both CD4+ and CD8+ cells by administering a **fusion protein** (FP') containing both **MHC**-I and -II epitopes fused to a CBE;
(h) producing **fusion proteins**; and
(i) secreting an intracellular or membrane protein (II) by introducing into a cell a vector (A'') similar to (A) but having the Ag-encoding sequence replaced by a (II)-encoding sequence so that a **fusion protein** is produced.
ACTIVITY - Cytotatic; antiviral; antibacterial; antifungal; antiprotozoal; anti-inflammatory; antiarthritic.
MECHANISM OF ACTION - Induction of specific **immune** response; gene therapy.
USE - (A) are used, directly or after transduction of antigen-presenting cells (APC), in vaccines for treatment and prevention of cancer, infections and autoimmune diseases. Vectors similar to (A), but expressing a test sequence rather than Ag, are used to identify polypeptides (PP) that contain **MHC**-II restricted epitopes for activation of CD4+ cells or elicitation of an **immune** response in vivo. PP (in APC) or vector containing DNA that expresses PP are useful for treating the above conditions.
ADVANTAGE - More efficient antigen presentation.
DESCRIPTION OF DRAWING(S) - The diagrams represent the retrogen strategy. The retrogen is produced in a cell (1A) and then taken up by an antigen presenting cell (APC) (1B). The retrogen is processed in and expressed upon the APC as a **MHC**-I or -II complex or is presented to B cell receptors (1A and 1B).
1A, 1B/26

TECH UPTX: 20001230
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Vector: The promoter may be constitutive, inducible or tissue-specific, e.g. the SV40 early, metallothionein or HER-2 promoters, and the SS is e.g. the **immunoglobulin** heavy chain leader sequence. The encoded Ag contains at least one epitope that induces a B cell, CD4+ or CD8+ cell response, especially all 3 responses, from one or more epitopes. Ag is associated with infectious diseases (viral, bacterial, fungal or protozoal), cancer or autoimmune diseases, e.g. hepatitis B or human **immune** deficiency virus, breast or cervical cancer, rheumatoid arthritis, Crohn's disease etc. CBD is a ligand that binds a cell-surface receptor, e.g. an Fc fragment, toxin cell-binding domain or cytokine, and may be homologous or heterologous. (A) may also include an integration signal sequence, e.g. a viral long terminal repeat, and is a viral, bacterial or mammalian vector.
Preferred Cells: Transformed cells of (a) are prokaryotic or eukaryotic (yeast, bacteria or mammalian cells).
Preparation: (A) are assembled by standard recombinant DNA methods.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Process: To elicit an **immune** response against Ag, (A) is introduced into a cell such that Ag is secreted, then undergoes endocytosis, intracellular processing and presentation to a cell-surface protein (CSP) to elicit a T cell-mediated **immune** response. CSP is an **MHC**-I or -II or B cell receptor and Ag is secreted from, and internalized by, different cells, especially both APC. (A) may be administered parenterally, directly to a mammal. Optionally (A) is administered together with a vector that expresses a cytokine. Alternatively a vector is used that encodes a cytokine and FP under control of a single promoter; or two (A) are administered expressing different Ag, or a single vector that expresses two different FP. In method (c), a vector, similar to (A) but having the

Ag-encoding sequence replaced by a test sequence, is introduced into an APC, then treated cells contacted with naive and primed T cells and any activation of these cells detected. Test sequences are cDNAs derived from tumor cell lines, pathogens or the human genome. Alternatively, the vector is administered parenterally to a mammal and spleen-derived T cells co-cultured with dendritic cells to identify any T cell activation. In method (g), the intracellular protein (particularly human papilloma virus 16 E7) or the membrane protein (particularly Epstein-Barr nuclear antigen-1) is truncated or modified to increase efficiency of secretion.

L25 ANSWER 7 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2000-451678 [39] WPIDS
DNC C2000-137528
TI **Immune** cells with predefined specificities useful for treating melanoma and **immune** diseases.
DC B04 D16
IN BOLHUIS, R L H; ESHHAR, Z; WILLEMSEN, R A
PA (BOLH-I) BOLHUIS R L H; (YEDA) YEDA RES & DEV CO LTD
CYC 24
PI WO 2000031239 A1 20000602 (200039)* EN 47p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA CN IL JP US
AU 2000012927 A 20000613 (200043)
ADT WO 2000031239 A1 WO 1999-IL622 19991118; AU 2000012927 A AU 2000-12927 19991118
FDT AU 2000012927 A Based on WO 200031239
PRAI IL 1998-127142 , 19981119
AB WO 200031239 A UPAB: 20000818
NOVELTY - **Immune** cells (I) with predefined specificity, produced by either complexing the cells with an antigen-specific major histocompatability complex (**MHC**)-restricted **T-cell receptor** (**TCR**) or transfecting the cells with an antigen specific **MHC**-restricted chimeric **TCR** gene, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) an **immune** cell (I), with a predetermined specificity, and which is either:

(a) complexed with an antigen specific major histocompatability complex (**MHC**)-restricted chimeric **T-cell receptor** (**TCR**) (or a fragment); or

(b) transfected with an antigen-specific **MHC**-restricted chimeric **TCR** gene; and

(2) a method (II) for the treatment of a tumor in a patient comprising complexing lymphocyte cells of the patient with an antigen specific **MHC**-restricted chimeric **TCR** (or fragment), or transfecting the autologous lymphocytes with an antigen-specific **MHC**-restricted chimeric **TCR** gene encoding a single chain **TCR** (scFv-**TCR**) which binds to an antigen associated with the tumor and a segment encoding a signal transducing element of an **immune** cell.

ACTIVITY - Cytostatic; antimicrobial; **immunosuppressive**.

To determine whether chimeric D scFv-, tc- and full length-TCRPOS T lymphocytes were able to recognize the MAGE-1 peptide, 51Cr labeled MAGE-1NEG, HLA-A1POS melanoma cells (MEL 2A) and EBV transformed B cell blasts (72-2 and APD) were pulsed with 10 mu g/ml MAGE-1 peptide or irrelevant influenza virus peptide derived from influenza virus A nucleoprotein and incubated for 6 hours with the chimeric scFv-TCRPOS T lymphocytes. T lymphocytes expressing chimeric 3D csFv-TCRs, chimeric tc-TCRs and full length alpha beta TCRs were able to lyze the MAGE-1

peptide loaded, MAGE-1NEG/HLA-A1POS MEL 2A melanoma cells and the MAGE-1NEG/HLA-A1POS B-lymphoid cell lines 72-2 and APD. Only MAGE-1 peptide pulsed MAGE-1NEG/HLA-A1POS target cells were specifically lyzed by the transduced T lymphocytes, but not the unloaded cells or the cells loaded with an irrelevant influenza peptide. Cytotoxicity analysis showed that HLA-APOS, MAGE-1POS melanoma cells are lyzed, by 3D scFv **TCR** V alpha V beta V beta CCkCD4Tm gamma POS T-lymphocytes as efficiently as by 3D scFv **TCR** V alpha V beta C beta zetaPOS T lymphocytes.

Preparation: (I) may be prepared by standard recombinant DNA methods.

MECHANISM OF ACTION - None given.

USE - Compositions comprising the **immune** cells (I) may be used for the treatment of cancer (especially melanomas (i.e. method (II), if the **TCR** binds to the melanoma-associated neoplastic protein (MAGE-1) antigen), infectious diseases, autoimmune disease and/or graft rejection (claimed).

ADVANTAGE - (I) have a predefined specificity.

Dwg.0/9

TECH UPTX: 20000818

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Cells: In (I), the chimeric **TCR** comprises:

(1) a segment (TCR1), comprising:

(a) a single chain **TCR** (scFv-**TCR**) comprised of the variable (VAR) region and (optionally) either the extracellular constant (CON) region of an antigen-specific **TCR** or the constant region of the **immunoglobulin** kappa light chain (Ck); or

(b) a 2 chain **TCR** (tcFv-**TCR**) made of the extracellular VAR and CON regions of an antigen-specific **TCR**; and

(2) a second segment (TCR2) comprising a signal transducing element of an **immune** cell.

The scFv-**TCR** or tcFv-**TCR** comprise the alpha and beta chains pair or the gamma and delta chain pair of an antigen-specific **TCR**. The single chain **TCR** of TCR1 is a 2 domain (2D) single chain **TCR** made of the extracellular VAR region ValphaVbeta chains of the antigen specific **TCR** linked by a linker. It may also be a 3D single chain **TCR** made of either the extracellular VAR and CON regions of the antigen specific **TCR** (the 3D single chain **TCR** comprises the ValphaVbetaVbeta or ValphaVbetaValpha chains of the antigen-specific **TCR**) or the extracellular VAR ValphaVbeta chains of the antigen-specific **TCR** and the CON region of the **immunoglobulin** kappa light chain (Ck).

If in (I), the TCR1 comprises a tcFv-**TCR** of the extracellular VAR and CON regions of the antigen specific **TCR**, then the tcFv-**TCR** comprises the ValphaCalpha and VbetaVbetachains of the antigen specific **TCR**.

TCR2 comprises a signal transducing element of an **immune** cell, comprising the intracellular signaling unit alone or together with the transmembrane domain and optionally with the extracellular domain of signaling chains. The signal transducing element is either the **TCR** /CD3 complex (gamma, delta, epsilon, eta or zeta (preferred)), the gamma chain of the Fc receptor (preferred), the alpha, beta and/or gamma subunit of the interleukin (IL) 2 receptor, the CD2, CD16, and/or CD28 co-receptor chains, the signaling elements of the natural killer (NK) receptor, killing inhibitory receptor (KIR) and/or killing activating receptor (KAR) and/or any signalling element derived from an **immune** cell.

The **immune** cell (I) is selected from resting, activating and memory T lymphocytes, cytotoxic lymphocytes (CTLs), helper T-cells, non-T lymphocytes, B cells (lymphocytes), plasma cells, natural killer (NK) cells, monocytes, macrophages, eosinophils and dendritic cells.(I) may be antigen specific or non-specific **immune** cells. The pre-defined specificity is targeted antigen uptake and presentation, increased

immunoglobulin production, increased antigen-presenting functions, increased lymphokine or cytokine production or target cell cytotoxicity (depending on the cell type).
Preferably, (I) is a target cell antigen-specific **immune** cell containing an antigen-binding molecule selected from alpha/beta chains or the gamma/delta chains of the antigen specific **T-cell receptor**, chimerized to a signal transducing element selected as described above.
In (I), the antigen binding molecule binds to viral, synthetic, tumor associated, tumor specific, mucosal, super, differentiation, self and/or auto-**immune** antigens, class I and/or II **MHC** molecules.
In particular the antigen binding molecule binds to the melanoma-associated neoplastic **protein** (MAGE-1) antigen.
The **chimeric** antigen-specific **TCR** (or fragment) is either bound to the **immune** cell by chemical conjugation or is bridged to the **immune** cell by a macromolecule or by a bispecific antibody binding to both the **TCR** and to the **immune** cell. The macromolecule is avidin, streptavidin or polylysine.
(I) may also be transfected with the antigen-specific chimeric **TCR** gene.
Preferred Methods: (II) is used for the treatment of a melanoma in a patient and comprises, transfecting lymphocyte cells of the patient with an antigen-specific **MHC**-restricted chimeric **TCR** gene containing a segment encoding a scFv-**TCR** which binds to the MAGE-1 antigen and a segment encoding a signal transducing element of an **immune** cell.

L25 ANSWER 8 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2000-339692 [29] WPIDS
DNN N2000-254984 DNC C2000-103145
TI New **fusion proteins** and gene constructs for expressing agents (antibodies, enzymes, vectors or molecular pathogenicides), useful for protecting plants against pathogens and increasing resistance to disease.
DC C06 D16 P13
IN EMANS, N; FISCHER, R; HOLZEM, A; LIAO, Y; MONECKE, M; NAEHRING, J; SACK, M; SCHILLBERG, S; SPIEGEL, H; ZIMMERMAN, S
PA (FRAU) FRAUNHOFER GES FOERDERUNG ANGEWANDTEN
CYC 23
PI WO 2000023593 A2 20000427 (200029)* EN 193p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: BR CA IN MX
EP 1123398 A2 20010816 (200147) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
BR 9915543 A 20010814 (200154)
ADT WO 2000023593 A2 WO 1999-EP7844 19991015; EP 1123398 A2 EP 1999-970685 19991015, WO 1999-EP7844 19991015; BR 9915543 A BR 1999-15543 19991015, WO 1999-EP7844 19991015
FDT EP 1123398 A2 Based on WO 200023593; BR 9915543 A Based on WO 200023593
PRAI IN 1998-666 19981016; EP 1998-119630 19981016
AB WO 200023593 A UPAB: 20000617
NOVELTY - A **fusion protein** (I) comprising at least one binding domain specifically recognizing an epitope of a plant pathogen and at least one further domain comprising a protein or peptide sequence which is toxic to the pathogen or detrimental to its replication, transmission or life cycle, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a pathogenicide (II) comprising (I) and a cellular targeting sequence and/or membrane localization sequence and/or motif that leads to

membrane anchoring; or at least one binding domain that specifically recognizes a viral movement and/or replicase protein;

(2) a polynucleotide (III) encoding (I) or (II);

(3) vectors (IV) comprising (II) or (III);

(4) a composition (V) comprising (IV), where the expression of at least two of the polynucleotides results in the production of (I) or (II), or their in vivo assembly;

(5) a host cell (VI) comprising (III), (IV) or (V);

(6) production of (II);

(7) a method (VII) for the production of pathogen resistant transgenic plants, plant cells or plant tissue comprising introducing the polynucleotide, or vectors into the genome of plant, plant cell or tissue;

(8) a transgenic plant cell (VIII), which contains stably integrated into the genome (III) or (IV);

(9) a transgenic plant (IX) or plant tissue (X) comprising (VIII);

(10) harvestable parts or propagation material of the plant (XI); and

(11) a kit (XII) comprising (I), (II), (III), (IV) or (V).

ACTIVITY - Pathogenicide; antimicrobial.

MECHANISM OF ACTION - Deoxyribonuclease; RNAse; ribosome inactivator; **immunomodulator**.

T1 progenies of plant line expressing the scFv24-PDGFR **fusion protein** (P9SR1) were inoculated with TMV. Seeds were collected from antibody-producing T0 plants and germinated. Kanamycin-resistant T1 plants were used for inoculation with TMV-v. Wild type N. tabacum cv. Petite Havana SR1 plants were used as a control. Disease symptoms were monitored 6 - 20 days post inoculation (p.i.) and for resistant plants up to 180 days p.i. Lower leaves were infected with TMV and systemic spread of the virus was followed by analyzing upper leaves 6-20 days later. All non-transgenic tobacco control plants were systemically infected, but 19% (out of 68 analyzed) of scFv24-PDGFR transgenic plants had no visible disease symptoms on the upper leaves. In 13% of scFv24-PDGFR transgenic plants no virus was found in the upper leaves up to 90 days post inoculation. Antibody-**fusion protein** expression levels correlated with expression of TMV resistance. Higher levels of scFv24 **fusion protein** expression led to an increased fraction of virus resistant plants.

USE - The **fusion protein**, pathogenicide, polynucleotide, vectors, compositions are useful for the protection of a plant against the action of a pathogen (claimed). The kit is useful for carrying out the methods and may be employed in different applications, for example in the diagnostic field or as research tools. The kit or its components, such as the **fusion protein**, pathogenicide, polynucleotides, vectors or compositions are useful in plant cell and plant tissue culture, in agriculture. They are extremely useful for breeding new varieties of plants that display improved properties such as resistance to pathogens.

ADVANTAGE - Current protective measures against pathogens rely heavily on chemical control measures for pathogen vectors, which have undesirable environmental consequences. Expressing genes (e.g. viral coat proteins, non-structural proteins of viral genomes, viral antisense transcripts, ribozymes or interferon genes) in transgenic plants in order to confer resistance have been effective for attenuating infections, but resistance was not complete and confined to a small spectrum of viral pathogens. Pathogen-specific recombinant antibodies targeted to different compartments of plant cells or different plant organs overcome these problems and confer a broader spectrum of resistance to disease. The methods, **fusion proteins**, polynucleotides, pathogenicide, compositions or vectors of the present invention provide protection to plants, in particular monocotyledonous and dicotyledonous agricultural crops and ornamental plants, against pathogens in a more

effective and environmentally sensitive manner.
Dwg.0/32

TECH UPTX: 20000617

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Protein: The domains may be linked by covalent or non-covalent bonds. Preferably, the binding domain comprises an antibody, a **T-cell receptor**, a pathogen specific receptor, a peptide specific for an epitope of a pathogen, or at least the binding site of any one of these. The antibody or its binding site is a recombinant full-size antibody, dimeric secretory IgA antibody, multimeric IgM antibody, F(ab')2 fragment, Fab-fragment, Fv-fragment, single chain Fv antibody (scFv), bispecific scFv, diabody, single domain antibody (dAb), minibody or molecular recognition unit (MRU). These may be derived from hybridoma cells, synthetic, semi-synthetic, naive and immunocompetent phage display or ribosome display libraries, or by the generation of fully synthetic designer antibodies. (I) preferably comprises at least two binding domains for the same or different epitope(s), where the epitopes are from the same or different pathogen(s). At least one of the domains may be fused to a C- or N-terminal carrier protein and at least one of the domains comprises a fluorophore. The toxic activity of the protein or peptide sequence is activated by the presence of a pathogen or host-specific peptide. The toxin is an enzyme or a viral structural or non-structural protein or a binding domain, selected from chitinase, glucanase, glucose oxidase, superoxide dismutase, DNAse, RNAse, RIP, lipase or their active fragments, either singly or in any combination(s).

Preferred Pathogenicide: Preferably, the membrane localization sequence, which comprises the pathogenicide, is proteolytically sensitive. Suitable membrane localization sequences, which enable the integration of secretory recombinant antibody **fusion proteins** and their parts in the plasma membrane, include the human **T cell receptor** transmembrane domains or any other member of the **immunoglobulin** superfamily, glyco-phosphatidyl inositol (GPI) anchors, KAR1, middle-T antigen, cytochrome b5 or syn1. Preferably, (II) comprises the **fusion protein**, and the binding domain(s) and/or further domain(s) are capable of self-assembly in vivo. (II) may also comprise an antibody. The pathogen may be a virus, bacterium, mycoplasma, fungus, nematode or insect.

Preferred Vector: (IV) may comprise separate polynucleotides encoding at least one of the binding domain(s) and/or the further domain(s) of the **fusion protein** or pathogenicide.

Preferred Polynucleotide: (III), which comprises (IV) and (V), is operatively linked to regulatory sequences that allow the expression of (I), (II) or their domains in a host cell. The regulatory sequence is a constitutive, chimeric, ubiquitous, tissue specific, organ specific or inducible promoter.

Preferred Plant: (I) or (II) of the transgenic plant are made functional against pathogens by in vivo assembly after co-transformation of at least two independent plant expression constructs. It may also be made functional after sexual crossing to form hybrid offspring from two parental plants expressing one or more of the domains of the **fusion protein** or the pathogenicide, or any other form of genetic recombination. The transgenic plant preferably displays improved resistance against a pathogen that the wild type was susceptible to.

Preparation: (I) composed of a pathogen-specific antibody and toxin molecule can be made by fusing the respective parts by genetic or biochemical means. (I) may be prepared by culturing (VI) and recovering the (I), (II) ot their domains from the medium.

L25 ANSWER 9 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 2000-171004 [15] WPIDS
DNC C2000-053140
TI Novel **fusion proteins** used to treat autoimmune disorders, e.g. multiples sclerosis, lupus, rheumatoid arthritis, scleroderma, diabetes or ulcerative colitis.
DC B04 D16
IN ZAGHOUANI, H
PA (UYTE-N) UNIV TENNESSEE RES CORP
CYC 87
PI WO 2000001732 A2 20000113 (200015)* EN 79p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9950908 A 20000124 (200027)
EP 1093464 A2 20010425 (200124) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000001732 A2 WO 1999-US15225 19990706; AU 9950908 A AU 1999-50908 19990706; EP 1093464 A2 EP 1999-935427 19990706, WO 1999-US15225 19990706
FDT AU 9950908 A Based on WO 200001732; EP 1093464 A2 Based on WO 200001732
PRAI US 1998-111123 19980706
AB WO 200001732 A UPAB: 20000323
NOVELTY - A **fusion protein** (I) for alleviating autoimmune symptoms comprises an **immunoglobulin** or portion linked to autoantigenic polypeptides or fragments, where the **immunoglobulin** is capable of Fc receptor binding and is endocytosed by an antigen presenting cell (APC), and the autoantigenic polypeptides provide **T cell receptor** peptide agonists for presentation on the APC surface upon endocytic processing.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method for alleviating symptoms associated with an autoimmune disorder in a patient, comprising administering (I) to the patient;

(2) a method for presenting multiple **T cell receptor** agonists on the surface of a professional or nonprofessional APC comprising:

(a) contacting (I) with at least one Fc receptor present on a surface of a professional or nonprofessional APC, the **fusion protein** being internalized by the APC; and

(b) endocytically processing the internalized **fusion protein** to provide more than one **T cell receptor** peptide agonist where the provided **T cell receptor** agonists are presented on the surface of the APC.

ACTIVITY - **Immunosuppressive**; Neuroprotective; Dermatological; Antiinflammatory; Antirheumatic; Antiarthritic; Antidiabetic; Antiulcer. A peptide (PLP1) derived from proteolipid protein (PLP) was used to form a **fusion protein** with **immunoglobulin** and used to treat experimental encephalomyelitis (EAE) in mice. EAE was induced in a group of 10 mice with 100 mu g of free PLP1 peptide. Soluble aggregated **Ig**-PLP1 was prepared by heating a solution of **Ig**-PLP1 for 15 minutes at 63 deg. C and then centrifuging and filtering the resulting preparation to remove any insoluble aggregates that were formed during the process. When the clinical signs of EAE started to develop at day 10 post disease induction, the mice were injected with a saline solution containing 300 mu g of the heat aggregated **Ig**-PLP1. A second and third injection of 300 mu

g of aggregated Ig-PLP1 were given at days 14 and 17 respectively. The results showed that aggregated arrangements of the disclosed **immunomodulating** agents may be used to effectively reduce the symptoms associated with **immune** disorders.

MECHANISM OF ACTION - Inhibitors of autoreactive T cells.

USE - (I) can be used for alleviating the symptoms associated with an autoimmune disorder, e.g. multiple sclerosis, lupus, rheumatoid arthritis, scleroderma, insulin-dependent diabetes and ulcerative colitis (claimed). Dwg.0/23

TECH UPTX: 20000323

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred protein: The **immunoglobulin** of (I) comprises at least part of a domain of a constant region of an **immunoglobulin** molecule, or a human IgG molecule. The autoantigenic polypetides or fragments of (I) comprise at least a portion of myelin basic protein and/or proteolipid protein. Preferred composition: The composition further comprises a pharmaceutical carrier. (I) is immobilized or aggregated. Preferred method: In the method of (2) the **T cell receptor** agonists are presented on the surface of the APC associated with at least one major **histocompatibility** complex (**MHC**). Preparation: The **fusion proteins** are preferably prepared by recombinant DNA techniques.

L25 ANSWER 10 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2000-072228 [06] WPIDS
DNC C2000-020588
TI Novel peptides for treating autoimmune diseases of central nervous system characterized by demyelination.
DC B04 D16
IN ARIMILLI, S; DESHPANDE, S
PA (CORI-N) CORIXA CORP
CYC 87
PI WO 9957241 A2 19991111 (200006)* EN 57p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9937890 A 19991123 (200016)
NO 2000005547 A 20010102 (200108)
EP 1080185 A2 20010307 (200114) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ZA 2000006268 A 20011031 (200173) 66p
CN 1308671 A 20010815 (200174)
ADT WO 9957241 A2 WO 1999-US9930 19990505; AU 9937890 A AU 1999-37890 19990505; NO 2000005547 A WO 1999-US9930 19990505, NO 2000-5547 20001103; EP 1080185 A2 EP 1999-920379 19990505, WO 1999-US9930 19990505; ZA 2000006268 A ZA 2000-6268 20001102; CN 1308671 A CN 1999-808248 19990505
FDT AU 9937890 A Based on WO 9957241; EP 1080185 A2 Based on WO 9957241
PRAI US 1998-73109 19980505
AB WO 9957241 A UPAB: 20000203

NOVELTY - An isolated peptide derived from human myelin basic protein (MBP), is new.

DETAILED DESCRIPTION - Novel MBP peptides have an amino acid (aa) sequence (S1):

Phe-X-Lys-Asn-Ile-Val-X-X-X-Thr-X-X (S1)

X = any aa.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid (I), encoding (1);

(2) a composition (II), comprising a major **histocompatibility** complex (**MHC**) class II complex (IIa) capable of binding a **T-cell receptor** (**TCR**), and (IIa) consisting of:

(a) a **MHC** class II polypeptide comprising an extracellular domain of a **MHC** class II molecule with an antigen (Ag) binding pocket, which is encoded by an allele associated with an autoimmune disease directed to MBP; and the class II component is soluble under physiological conditions in the absence of detergent or liquid;

(b) a MBP peptide having an aa sequence (S2); and

(c) the MBP peptide is bound to **MHC** class II component Ag binding pocket;

(3) an antibody (Ab) specifically immunoreactive under immunologically active conditions to a MBP peptide having an amino acid sequence (S3);

(4) a composition comprising (II); and

(5) identifying a T-cell epitope on an Ag which when bound to the Ag binding pocket of a **MHC** class II molecule, is capable of binding to a **TCR** and such binding triggers an extracellular acidification reaction by a T-cell expressing the **TCR**, by:

(a) providing a composition comprising the T-cell epitope bound to the Ag binding pocket of a **MHC** class II molecule;

(b) contacting a T-cell expressing the **TCR**, with the epitope; and

(c) measuring the extracellular acidification, in which a change in the extracellular acidification indicates the binding of T- cell epitope to the **TCR**.

Phe-X-Lys-R1-Ile-Val-X-X- X-Thr-X-X (S2)

R1 = Asn or Gln.

Phe-Phe-Lys-Asn-Ile-Val-Thr-Pro-Arg-Thr- Pro-Pro (S2)

ACTIVITY - Neuroprotective. No supporting data given.

MECHANISM OF ACTION - T-cell clonal anergy/tolerance inducer; Cytokine-mediated **immunosuppressive immune** response inducer.

USE - The MBP peptides are used in the treatment of autoimmune mediated demyelinating disease especially multiple sclerosis or the murine demyelinating experimental autoimmune encephalomyelitis. The therapeutic compositions comprising novel MBP peptides are used for inducing oral tolerance or general tolerance. The compositions are used to downregulate or eliminate autoreactive components of the **immune** system and treat autoreactive demyelinating, T-cell mediated **immune** response. The novel MBP peptides when administered into a subject are useful for inhibiting a T-cell mediated **immune** response against MBP, to treat the T-cell mediated **immune** response which causes a pathological condition of the nervous system e.g., multiple sclerosis (claimed).

ADVANTAGE - Prevention or suppression of **MHC**-restricted **immune** responses is done without any undesirable side effects, such as nonspecific suppression of an individual's overall **immune** response. The MBP peptides provide a safer and more effective treatment by selectively suppressing autoimmune responses at the helper CD4+ T-cell levels.

Dwg.0/8

TECH UPTX: 20000203

TECHNOLOGY FOCUS - BIOLOGY - Isolation: The **MHC** class II polypeptides are isolated from any cell expressing the class II molecule of interest such as e.g., B or T lymphocytes from an individual with the appropriate genotype, such as one suffering from demyelinating autoimmune disease.

Preparation: The polyclonal Abs and monoclonal Abs are synthesized by standard methods described in Sites (eds.) Basic And Clinical Immunology (7th ed.) Lange Medical Publications, Goding, Monoclonal Antibodies: principles And Practice (2d ed.) Academic Press, New York, NY (1986) etc.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: The MBP peptides and **MHC** class II polypeptides are prepared by standard solid phase chemical synthesis or by automated synthesis using the ABI 431A peptides synthesizer.
Preferred Method: The MBP peptide or **MHC** class II polypeptide: MBP peptide complexes are modified to alter their pharmacokinetics and biodistribution by substantially removing all of the carbohydrate moieties, for increasing serum half-life of the complexes since carbohydrates are involved in the elimination of the complexes from the bloodstream. These complexes are protected in vesicles composed of lipids e.g., liposomes. The peptide portion and the **MHC** sub unit components are non- covalently associated by contacting the peptide with the **MHC** sub unit component by e.g., mixing. The effector is then covalently linked. Water solubility of the class II peptide complexes can be engineered by deleting the transmembrane domain (typically hydrophobic) aa residues. This is most effectively accomplished by recombinantly redesigning the DR allele to substitute hydrophobic residues with hydrophilic residues and expressing the truncated class II molecule.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: The MBP peptide and **MHC** class II polypeptides are synthesized by recombinant methods.
Preferred Peptides: The isolated MBP peptides encoded by (I) have an aa sequence of (S3) or an aa sequence of (S2) which has undergone conservative substitutions. The peptide may be linked to a heterologous sequence and so is a **fusion protein**, which facilitates cell killing, protein detection, purification, or other applications. Detection and purification facilitating domains include, e.g., metal chelating peptides such as polyhistidine tracts and histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized **immunoglobulin**, and the domain utilized in the FLAGS extension/affinity purification system.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: (II) has a MBP peptide with an aa sequence (S3) or an aa sequence (S2) which has undergone conservative substitutions and is a **fusion protein** and further comprises a effector composition. The effector portion of the molecule can be, e.g., a toxin, a chemotherapeutic agent, an Ab to a cytotoxic T lymphocyte (CTL) surface molecule, a lipase, or a toxic radioisotope emitting, e.g., gamma radiation from radioisotopes such as yttrium-90, phosphorus-32, lead-212, iodine-131, or palladium-109. The toxins used are ricin, diphtheria, gelonin, Pseudomonas toxin, and abrin. The chemotherapeutic agents used are doxorubicin, daunorubicin, methotrexate, cytotoxin, and anti-sense RNA. This composition is for autoimmune diseases and is directed to MBP in multiple sclerosis. The **MHC** class II polypeptide in the composition comprises the Ag binding pocket of an HLA DR2 (II) and has the transmembrane region of class II sub unit included in it.
TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Method: Identification of the T-cell epitope is carried out by measuring the change in extracellular acidification using a microphysiometer. The microphysiometer measures the acidity of the principal catabolic products in mammalian cells, lactate and carbon dioxide. Very small changes in the acidity of the cultural medium bathing a small sample of cells can be readily determined with a light addressable potentiometric sensor. The rate of acidification is used as a measure of catabolic rate of the cells

being assayed. The **immunosuppressive** capability of an MBP peptide or class II:MBP peptide complex can be evaluated by first adding a complex to an autoreactive T-cell/ antigen presenting cell (APC) culture followed by MBP peptide challenge. Lack of or a relative decrease in cell activation indicative of **immunosuppression**, can be measured by a lessening or lack of extracellular acidification.

L25 ANSWER 11 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1999-418295 [35] WPIDS
CR 1995-393086 [50]; 1998-192827 [17]
DNC C1999-122844
TI Epstein-Barr virus BZLF2 proteins.
DC B04 D16
IN ALDERSON, M; ARMITAGE, R J; COHEN, J I; COMEAU, M R; FARRAH, T M; HUTT-FLETCHER, L M; SPRIGGS, M K
PA (IMMV) IMMUNEX CORP
CYC 1
PI US 5925734 A 19990720 (199935)* 25p
ADT US 5925734 A CIP of US 1994-235397 19940428, Div ex US 1995-430633 19950428, US 1997-936854 19970924
FDT US 5925734 A Div ex US 5726286
PRAI US 1995-430633 19950428; US 1994-235397 19940428; US 1997-936854 19970924
AB US 5925734 A UPAB: 19990902
NOVELTY - Epstein-Barr virus BZLF2 proteins capable of binding to a beta chain of a Class II major **histocompatibility** complex antigen to inhibit an antigen-specific response are new.
DETAILED DESCRIPTION - Independent claims are included for:
(1) an isolated **fusion protein** comprising a BZLF2 **protein** selected from the group consisting of a protein comprising:
(a) amino acids 34 - 223 of a sequence (I), which comprises 223 amino acids as defined in the specification;
(b) amino acids 60 - 223 of (I);
(c) amino acids 91 - 223 of (I);
(d) amino acids 123 - 223 of (I);
(e) fragments of (a) to (d) that bind the **MHC** Class II beta chain, and either
(f) a domain selected from an **immunoglobulin** Fc, mutein, or
(g) an oligomerising zipper domain, and
(2) a composition comprising a BZLF2 **fusion protein** together with a suitable dilutent or carrier.
ACTIVITY - Antiinflammatory; antiasthmatic; **immunosuppressive**.
MECHANISM OF ACTION - Vaccine.
USE - BZLF2 is useful for inhibiting antigen-specific antibody formation, the proliferation of blood mononuclear mononuclear cells, and cytotoxic T cell responses.
BZLF2 is also useful for inhibiting undesirable antigen specific responses, e.g. in the treatment or prevention of asthma; for preventing or treating autoimmune disease; and for preventing tissue or organ transplant rejection.
Dwg.0/5
TECH UPTX: 19990902
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Fc Region: The Fc region comprises amino acids 1 - 213 of a 212 amino acid sequence as given in the specification.

L25 ANSWER 12 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 1999-384758 [32] WPIDS
DNC C1999-113101
TI **Immunomodulating fusion proteins** that may be used to mediate **immune** responses.
DC B04 D16
IN LOEWENADLER, B; LYCKE, N
PA (LOEW-I) LOEWENADLER B; (LYCK-I) LYCKE N
CYC 1
PI US 5917026 A 19990629 (199932)* 12p
ADT US 5917026 A US 1996-596482 19960205
PRAI US 1996-596482 19960205
AB US 5917026 A UPAB: 19990813
NOVELTY - DNA sequence (I) encoding a **fusion protein** that can be targeted to a specific cell receptor, is new.
DETAILED DESCRIPTION - The (I) encodes a water soluble **fusion protein** that comprises:
(a) a sequence (S1) encoding the A1 subunit of cholera toxin (CT) or Escherichia coli heat labile enterotoxin (LT); and
(b) a sequence (S2) encoding a peptide which specifically binds to a receptor expressed on a lymphocyte, macrophage, dendritic cell, Langerhans cell, or epithelial cell capable of expressing **MHC** Class I or II antigens.
INDEPENDENT CLAIMS are also included for the following:
(1) the protein encoded by (I);
(2) a **fusion protein** which comprises the A1 subunit of CT fused to at least 1 copy of protein A or a protein A fragment;
(3) a transformed bacterial cell expressing (I); and
(4) a vector expressing (I).
USE - Proteins encoded by (I) may be used to mediate the **immune** response in inflammation, autoimmunity, and allergies, to enhance tumor **immunity** and increase the efficiency of vaccine take to prevent organ transplant rejection, and treat diseases in which the **immune** system is part of the pathogenic mechanism or important for host resistance.
DESCRIPTION OF DRAWING(S) - The diagram shows a schematic representation of pKP1001.
Dwg.2/2
TECH UPTX: 19990813
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Toxin: The bacterial toxin is the A1 subunit of CT.
Preferred Cell: The antigen presenting cell is a B-lymphocyte.
Preferred Receptor: The peptide encoded by S2 specifically binds to an **Ig** or Fc receptor. The receptor binding peptide is Staphylococcus protein A, or a protein A fragment or monomer, and is preferably a dimer of the D region of protein A.

L25 ANSWER 13 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1999-357351 [30] WPIDS
DNC C1999-105653
TI New immunogenic compositions for treating cancer or virus or parasite infection.
DC A96 B04 D16
IN BRASLAWSKY, G R; HANNA, N; HARIHARAN, K; HARIHARA, K
PA (IDEC-N) IDEC PHARM CORP
CYC 84
PI WO 9913912 A1 19990325 (199930)* EN 41p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE

GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW

ZA 9808461 A 19990630 (199931) 36p
AU 9895658 A 19990405 (199933)
EP 1015031 A1 20000705 (200035) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
NO 2000001413 A 20000518 (200035)
CN 1279616 A 20010110 (200128)
US 2001018054 A1 20010830 (200151)
US 2001019715 A1 20010906 (200154)
KR 2001024109 A 20010326 (200161)
JP 2001516727 W 20011002 (200172) 32p

ADT WO 9913912 A1 WO 1998-US18495 19980917; ZA 9808461 A ZA 1998-8461 19980916; AU 9895658 A AU 1998-95658 19980917; EP 1015031 A1 EP 1998-949313 19980917, WO 1998-US18495 19980917; NO 2000001413 A WO 1998-US18495 19980917, NO 2000-1413 20000317; CN 1279616 A CN 1998-811280 19980917; US 2001018054 A1 Cont of US 1997-933359 19970918, US 2001-853580 20010514; US 2001019715 A1 Div ex US 1997-933359 19970918, US 2001-853581 20010514; KR 2001024109 A KR 2000-702864 20000317; JP 2001516727 W WO 1998-US18495 19980917, JP 2000-511527 19980917

FDT AU 9895658 A Based on WO 9913912; EP 1015031 A1 Based on WO 9913912; JP 2001516727 W Based on WO 9913912

PRAI US 1997-933359 19970918; US 2001-853580 20010514; US 2001-853581 20010514

AB WO 9913912 A UPAB: 19990802

NOVELTY - New immunogenic compositions for treating cancer or virus or parasite infection comprise a combination of antigen formulation and an agent capable of neutralizing or down-regulating **immunosuppressive** factors.

DETAILED DESCRIPTION - A composition (A) comprises:

(a) an admixture comprising a cancer, viral or parasitic antigen expressed by cancer, virally or parasitic infected cells and a microfluidized antigen formulation (MAF) (formulated as a stable oil-in-water emulsion), the antigen formulation comprising:

(i) a stabilizing detergent;

(ii) a micelle-forming agent; and

(iii) a biodegradable and biocompatible oil; and

(b) at least one agent which is capable of neutralizing or down-regulating the activity of **immunosuppressive** factors.

INDEPENDENT CLAIMS are also included for the following:

(1) a method of treatment which includes the induction of a cytotoxic T-lymphocyte (CTL) response where the improvement comprises:

(a) the administration of an adjuvant which induces a CTL response; and

(b) the administration of an antagonist of an **immunosuppressive** factor, where the administration of adjuvant and antagonist is effected sequentially or concurrently, and in any order;

(2) a method of restoring or boosting hematopoiesis comprising administering to a patient:

(a) an admixture as in (A) (a) which is administered to the patient to induce a CTL response in the patient which is specific for the viral or cancer antigen contained in the admixture; and

(b) at least one agent which is capable of neutralizing or down regulating the activity of tumor and host secreted **immunosuppressive** factors, where the admixture and the agent are administered separately or in combination, and in any order;

(3) a composition comprising an admixture as in (A) (a) and one or more transforming growth factor (TGF) beta antagonists;

(4) treatment of neoplastic or cancerous growths, comprising:

(a) administration of an admixture comprising a cancer or tumor antigen expressed by the cancer cells and a MAF (described above); and

(b) administration of at least one agent which is capable of neutralizing or down-regulating the activity of tumors and host secreted **immunosuppressive** factors. The admixture is administered in an amount sufficient to induce a cytotoxic T-lymphocyte response in the patient which is specific for the cancer or tumor antigen contained in the admixture.

ACTIVITY - Antitumor; Antiviral; Antiparasitic.

MECHANISM OF ACTION - Induction of a cytotoxic T-lymphocyte response.

USE - The methods can be used for restoring or boosting hematopoiesis (claimed). They can be used for treating cancers, e.g. breast cancer, brain cancer, cervical cancer, leukemia, lymphoma, prostate cancer, skin cancer, bladder cancer, kidney cancer, myeloma, colorectal cancer, or endometrial cancer, viral infections e.g. papillomavirus, hepatitis, herpes, cytomegalovirus, respiratory syncytial virus or HIV, or parasitic infection, e.g. malaria (claimed). The agent which is capable of neutralizing or down-regulating the activity of **immunosuppressive** factors enhances the efficacy of tumor/viral vaccines.

ADVANTAGE - The combinations of the antigen compositions and antagonists of **immunosuppressive** agents results in a synergistic enhancement of CTL response, thereby resulting in enhanced therapeutic response against targeted antigen-expressing cells.

Dwg.0/4

TECH UPTX: 19990802

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Composition: The detergent may be e.g. Tween 80 (RTM), Tween 20 (RTM), Tween 40 (RTM), Tween 60 (RTM), Zwittergent 3-12 (RTM), Teepol HB7, or SPAN 85. The amount of detergent is 0.05-0.5%.

The micelle-forming agent has a hydrophilic-lipophilic balance of 0-2 and may be e.g. Poloxamer 401 (RTM), Puronic L62Lf (RTM), Pluronic L101 (RTM), Pluronic L64, PEG1000 (RTM), Tetronic 1501 (RTM), Tetronic 150R1 (RTM), Tetronic 701 (RTM), Tetronic 901, Tetronic 1301, Tetronic 130R1 (RTM). The amount of this agent is 0.5-10%.

The oil has a melting point of below 65degreesC and may be e.g. squalene, eicosane, tetratetracontane, pristane, or a vegetable oil (especially olive oil). The amount of oil is 2.5-5%.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Composition: The **immunosuppressive** factor is transforming growth factor beta (TGFbeta).

The agent which is capable of neutralizing or down-regulating the activity of tumor or host secreted **immunosuppressive** factors may be e.g. an anti-TGF-beta antibody, a TFGbetaR-**fusion protein**, a TGF-beta analog, a TGF-beta binding protein, a TGF-betaR blocking antibody, a thrombospondin peptide, a TFGbetaR Fc-**fusion protein**. The antigen may be e.g. gp100, MART-1/Melan A, gp75, tyrosinase, melanoma proteoglycan, MAGE, BAGE, GAGE, RAGE, N-acetylglucosaminyltransferase-V, mutated beta-catenin, mutated MUM-1, mutated cyclin dependent kinases-4, p21 ras, BCR-abl, p53, p185 HER2/neu, mutated epidermal growth factor receptor, carcinoembryonic antigens, carcinoma associated mutated mucins, EBNA gene products, papillomavirus E7 protein, papillomavirus E6 protein, prostate specific antigens, prostate specific membrane antigen, PCTA-1, **immunoglobulin** idiotypes or **T cell receptor** idiotypes.

L25 ANSWER 14 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1999-229239 [19] WPIDS
DNN N1999-169623 DNC C1999-067440
TI Rin2 polypeptides and related nucleic acid.

DC B04 D16 S03
IN GALLI, S J; TAM, S; TSAI, M
PA (BETH-N) BETH ISRAEL DEACONESS MEDICAL CENT
CYC 22
PI WO 9913079 A1 19990318 (199919)* EN 101p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US
AU 9893156 A 19990329 (199932)
US 5965707 A 19991012 (199949)
ADT WO 9913079 A1 WO 1998-US19056 19980911; AU 9893156 A AU 1998-93156 19980911; US 5965707 A Provisional US 1997-58520P 19970911, US 1997-942819 19971002
FDT AU 9893156 A Based on WO 9913079
PRAI US 1997-942819 19971002; US 1997-58520P 19970911
AB WO 9913079 A UPAB: 19990518
NOVELTY - Isolated Rin2 polypeptides (I) which downregulate functional responses elicited by Ras-dependent signaling pathways, and their active derivatives and fragments.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) isolated nucleic acid (II) that encodes (I);
(2) DNA constructs containing (II) plus regulatory sequences;
(3) recombinant host cells containing this construct;
(4) production of recombinant (I) by culturing these cells;
(5) antibody, or its antigen-binding fragments, that binds specifically to (I);
(6) method for identifying agents (A) that alter activity of (I); and
(7) (A) identified this way.

ACTIVITY - anti-allergic; antiproliferative; anticancer; antidiabetic; anti-arthritic; anti-inflammatory; angiogenic; cell-proliferative.

MECHANISM OF ACTION - Ras-dependent signaling is involved in release of mediators from mast cells; T cell function, and cell proliferation. (A) modulate this signaling (or functional responses dependent on it) in cells that express an appropriate receptor, particularly a Fc epsilon RI, TrkA (for nerve growth factor), c-kit or **T cell receptor**, with functional responses being:

(1) activation of Erk-MAP, JNK or p39 MAP kinases;
(2) cellular secretion (particularly of preformed or lipid mediators and/or cytokines). cDNA encoding murine Rin2 was cloned, in antisense orientation, into pBK-CMV and the plasmid used to transform C1.MC/C57.1 murine mast cells.

When the Fc epsilon RI receptor was activated (crosslinked) in the transformed cells, activation of Erk-MAP kinase was strongly potentiated (after 30 min, about double the activity of cells transformed with empty pBK-CMV). JNK and p39 MAP kinase were also potentiated.

USE - Agents that increase Rin2 activity (particularly Rin2 itself, optionally expressed from a vector) are used to treat allergy (asthma, hayfever or atopic eczema); Ras-dependent cancers and (non-)neoplastic cellular proliferation; autoimmune diseases; T cell-associated diseases and T cell dependent graft vs. host disease (typical examples being type I diabetes mellitus; multiple sclerosis, Crohn's disease, autoimmune hepatitis and psoriasis).

Agents that inhibit Rin2 activity are used to improve wound healing; angiogenesis and/or re-epithelialization (also to improve **immune** response to pathogens; in human **immune** deficiency virus, and some other, infections; **immune** suppression associated with cancer therapy, and nerve regeneration).

(I) is useful as molecular weight marker, to raise specific antibodies and therapeutically.

(II) is used to express recombinant (I); as antisense molecules for reducing Rin2 expression; to identify Rin2 gene mutations and to identify proteins that bind specifically to Rin2 (in two-hybrid assays). Antibodies specific for (I) are used to detect (I) in cells or lysates by standard immunoassays, also as Rin2 inhibitors and reagents for studying Ras-effector pathways.
Dwg.0/15

TECH UPTX: 19990510
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred polypeptides: (I) particularly down regulates FcepsilonRI aggregation and has a 491 amino acid (aa) sequence (Ia) given in the specification, or is at least 40% similar to (Ia). Preferred nucleic acid: (II) is a 2664 bp sequence (IIa), encoding (Ia), or its fragment or derivative, particularly a fragment extending from nucleotides 51-405; 532-1276; 885-1144 or containing the 822 3'-terminal bp of (IIa), or their complements, derivatives or fragments. (I) may also be any sequence with at least 75, preferably 90,% identity with (IIa) or the specified fragments.
Preferred assay: To identify (A), a cell containing (I) is subjected to a stimulus that activates at least one Ras-dependent pathway in the cell, in presence and absence of test compound, and any alteration of (I) activity detected. The stimulus is particularly nerve growth factor, stem cell factor; peptide antigen and major **histocompatibility** molecules, or **immunoglobulin** E (IgE) plus specific antigen. Typical compounds for testing are Rin2 derivatives or mimics.
Preparation: (I) can be isolated from natural sources and antibodies are produced by usual immunization or cell fusion techniques.
Cells of the growth factor-independent murine mast cell line C1.MC/C57.1 were sensitized to anti-DNP (dinitrophenyl) IgE, then challenged with hapten and total RNA extracted at various times from both stimulated and unstimulated cells. Conventional differential display analysis was performed to identify a clone (60-4, 382 bp) that was expressed in activated cells. This was used as probe to screen a mouse mast cell cDNA library to identify clone SY-6 containing a 1.1 kb insert. This was used to screen a mouse brain library to isolate a clone, SY-A, containing sequence (Ia). Once identified this sequence may be expressed in standard vector/host cell systems, in sense or antisense orientations, e.g. for expression of Rin2 polypeptides, optionally as **fusion proteins**. The sequences was also used to isolate the corresponding human cDNA.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) can be synthesized by standard chemical methods.

L25 ANSWER 15 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1998-609990 [51] WPIDS
DNC C1998-182822
TI Leukocyte **immunoglobulin**-like receptor, LIR, polypeptides - useful, e.g. for treating autoimmune diseases or disease states associated with suppressed **immune** function.
DC B04 D16
IN COSMAN, D J
PA (IMMV) IMMUNEX CORP
CYC 73
PI WO 9848017 A1 19981029 (199851)* EN 112p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AU BA BB BG BR CA CN CU CZ EE GE HU IL IS JP KP KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK SL TR TT UA US UZ VN YU
AU 9871547 A 19981113 (199913)
EP 977852 A1 20000209 (200012) EN

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ES 2143450 T1 20000516 (200031)
JP 2001523099 W 20011120 (200204) 160p
ADT WO 9848017 A1 WO 1998-US8244 19980423; AU 9871547 A AU 1998-71547 19980423; EP 977852 A1 EP 1998-918667 19980423, WO 1998-US8244 19980423; ES 2143450 T1 EP 1998-918667 19980423; JP 2001523099 W JP 1998-546353 19980423, WO 1998-US8244 19980423
FDT AU 9871547 A Based on WO 9848017; EP 977852 A1 Based on WO 9848017; ES 2143450 T1 Based on EP 977852; JP 2001523099 W Based on WO 9848017
PRAI US 1997-842248 19970424
AB WO 9848017 A UPAB: 19981223
New leukocyte **immunoglobulin**-like receptor (LIR) polypeptides: (i) have at least 77 % identity to amino acids 5-50 of 650 amino acid sequence (S1); (ii) comprise amino acid sequence (S2); (iii) are encoded by DNA hybridising under high stringency (hybridising temperature at least 63 deg. C) to probe comprising nucleotides 310-1684 of 2922 bp sequence (S3) or to sequence complementary to probe; (iv) are encoded by DNA hybridising under high stringency (hybridising temperature at least 68 deg. C) to 30 or 52 bp sequence (S4) or (S5); (v) soluble polypeptide comprising sequence at least 90% identical to: (a) extracellular domain of LIR family members, comprising amino acids 1- or 17-458 of sequence (S1) or specified regions of nine other sequences, or (b) fragments of such extracellular domains capable of binding a ligand: Leu Xaa1 Leu Ser Xaa2 Xaa3 Pro Arg Thr Xaa4 Xaa5 Gln Xaa6 Gly Xaa7 Xaa8 Pro Xaa9 Pro Thr Leu Trp Ala Glu Pro Xaa10 Ser Phe Ile Xaa10 Xbb Ser Asp Pro Lys Leu Xaa11 Leu Val Xaa12 Thr Gly (S2) Xaa1=Gly or Arg; Xaa2=Leu or Val; Xaa3=Gly or Asp; Xaa4=His, Arg or Cys; Xaa5=Val or Met; Xaa6=Ala or Thr; Xaa7=His, Pro or Thr; Xaa8=Leu, Ile or Phe; Xaa9=Gly, Asp or Ala; Xaa10=Thr, Ile, Ser or Ala; Xaa11=Gly or Val; Xaa12=Met or Ala, and Xbb=sequence of 70 amino acids Also claimed are: (1) DNA encoding LIR polypeptide as above, or LIR polypeptide with sequence at least 90 % identical to (S1) or nine other sequences; (2) expression vector comprising DNA encoding polypeptide of (i); (3) host cells comprising (2); (4) antibody immunoreactive with polypeptide of (i); (5) **fusion protein** comprising amino acids 17-458 of (S1) and Fc region of **Ig**, and (6) fusion DNA construct comprising DNA encoding (5) (11 sequences are given in the specification).

USE - The polypeptides can be administered therapeutically, especially by expressing encoding DNA, to treat disorders associated with insufficient/defective amounts of LIR polypeptide. They may be included in pharmaceutical compositions (e.g. comprising polypeptide of (i) combined with a suitable carrier; claimed) useful for such administration. LIR-P3G2 and certain other LIR family members contain cytoplasmic immunoreceptor tyrosine-based inhibitory motifs (ITIMs), whilst other LIR family members lack ITIMs. By analogy with the structure and function of known **MHC** Class I receptor molecules, LIRs having ITIMs are inhibitory receptors mediating negative signalling, whilst those lacking ITIMs are activatory receptors. Failure of a receptor that mediating negative signalling could result in autoimmune diseases, whilst failure of a receptor mediating activatory signalling could result in suppressed **immune** function. The polypeptides can therefore be used to isolate ligands and produce antibodies which are useful to treat autoimmune diseases or disease states associated with suppressed **immune** function, depending on the polypeptide involved. Thus agonistic antibodies/ligands can be used to downregulate a cell function in conditions in which the **immune** system is overactive and excessive inflammation/immunopathology occurs, and antagonistic antibodies to activate a specific **immune** function in conditions associated with suppressed **immune** functions when the LIR comprises an ITIM. Conversely, agonistic antibodies or ligands may be used to activate

immune functions and antagonistic antibodies for **immune** suppression when the LIR lacks an ITIM. LIR-specific antibodies are also useful to detect or purify LIR polypeptides. The DNA sequences are useful to produce antisense sequences for therapeutic administration to modulate/prevent LIR expression e.g. to treat/prevent conditions as above. They are also useful to produce probes for detecting LIR nucleic acids or isolating LIR DNA from other species.
Dwg.0/0

L25 ANSWER 16 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1996-287183 [29] WPIDS
DNC C1996-091888
TI Isolated Herpes virus Saimiri 14 proteins - useful for treating autoimmune disorders, transplant rejection, allergy, asthma, cancer or viral disease.
DC B04 D16
IN ALDERSON, M; ARMITAGE, R; SPRIGGS, M; YAO, Z; ARMITAGE, R J; SPRIGGS, M K
PA (IMMV) IMMUNEX CORP
CYC 25
PI WO 9617939 A1 19960613 (199629)* EN 45p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA FI JP KR MX NO NZ
AU 9644190 A 19960626 (199641)
US 5716623 A 19980210 (199813) 22p
ADT WO 9617939 A1 WO 1995-US15948 19951207; AU 9644190 A AU 1996-44190 19951207; US 5716623 A CIP of US 1994-351901 19941207, US 1995-485549 19950606
FDT AU 9644190 A Based on WO 9617939
PRAI US 1995-485549 19950606; US 1994-351901 19941207
AB WO 9617939 A UPAB: 19960724
Isolated and substantially homogeneous viral protein capable of binding to a **MHC** Class II mol., selected from proteins encoded by a Herpes virus Saimiri 14 (HVS14) ORF, is claimed. Also claimed are: (1) isolated and substantially homogenous **fusion protein**, comprising amino acids 34-249 of the 249 residue HVS 14 sequence given in the specification; (2) isolated and substantially homogeneous **fusion protein** comprising HSV 14 **protein** of (1), and a **immunoglobulin** Fc region, or oligomerising zipper domain; and (3) preventing or treating an undesirable, antigen-specific **immune** or inflammatory response, comprising administering a HVS 14 compsn. to an individual.
USE - The HVS 14 protein can inhibit antigen presentation, or can act as a superantigen. It can be used to prevent or treat autoimmune disorders, tissue or organ transplant rejection and allergy or asthma. HSV14 **fusion proteins** can be used to treat cancer or viral disease. The HVS14 protein can also be used as a reagent in in vitro assays, as an immunogen or as a binding agent.
Dwg.0/5

L25 ANSWER 17 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1995-393086 [50] WPIDS
CR 1998-192827 [17]; 1999-418295 [35]
DNC C1995-169371
TI Epstein-Barr virus BZLF2 **fusion proteins** - used for treating e.g. auto-**immune** disease, transplant rejection, allergy, asthma, cancer or viral infection..
DC B04 D16
IN ALDERSON, M; ARMITAGE, R J; COHEN, J I; COMEAU, M R; FARRAH, T M; HUTT-FLETCHER, L M; SPRIGGS, M K
PA (IMMV) IMMUNEX CORP; (UMOR) UNIV MISSOURI; (USSH) US NAT INST OF HEALTH
CYC 24

PI WO 9530015 A2 19951109 (199550)* EN 51p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA FI JP KR MX NO NZ
ADT WO 9530015 A2 WO 1995-US5348 19950428
PRAI US 1994-235397 19940428
AB WO 9530015 A UPAB: 19990902
(A) An isolated and homogeneous viral protein is claimed which is capable of binding a beta chain of a Major **HIstocompatibility** Complex (**MHC**) Class II antigen and is selected from proteins encoded by a BZLF2 open reading frame (ORF) of an Epstein-Barr virus (EBV). Also claimed are: (B) an isolated and homogeneous **fusion protein** (FP) comprising a BZLF2 protein as in (A) and a domain selected from an **immunoglobulin** (**Ig**) Fc region and an **Ig** Fc mutein; and (C) an isolated and homogeneous FP comprising a BZLF2 protein as in (A) and an oligomerising zipper domain (OZD).
USE - The BZLF2 proteins inhibit antigen-specific antibody formation, proliferation of peripheral blood mononuclear cells and cytotoxic T cell responses and also exhibit superantigen-like activity. They can be used for treating or preventing autoimmune diseases such myasthenia gravis, multiple sclerosis and systemic lupus erythematosis, for treating organ or tissue transplant rejection and for treating or preventing allergy or asthma. They can also be used for treating cancer and viral disease, esp. EBV infection.
Dwg.0/5

L25 ANSWER 18 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1994-294333 [36] WPIDS
DNC C1994-134228
TI Treating and preventing autoimmune disease with soluble **T cell receptor** alpha chain - from suppressor T cell opt. fused to a **immunoglobulin** constant region, effective against a wide range of diseases..
DC B04 D16
IN TANIGUCHI, M; WATANABE, H; YAMAGATA, N
PA (FARH) HOECHST JAPAN LTD; (FARH) HOECHST JAPAN KK
CYC 22
PI WO 9419470 A1 19940901 (199436)* JA 27p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA KR US
AU 9460428 A 19940914 (199502)
JP 06298662 A 19941025 (199502) 8p
EP 667908 A1 19950823 (199538) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE
US 5648332 A 19970715 (199734) 8p
AU 686134 B 19980205 (199813)
CA 2134083 C 20000627 (200043) EN
ADT WO 9419470 A1 WO 1994-IB29 19940222; AU 9460428 A AU 1994-60428 19940222; JP 06298662 A JP 1993-179062 19930720; EP 667908 A1 EP 1994-906987 19940222, WO 1994-IB29 19940222; US 5648332 A WO 1994-IB29 19940222, US 1994-318881 19941020; AU 686134 B AU 1994-60428 19940222; CA 2134083 C CA 1994-2134083 19940222, WO 1994-IB29 19940222
FDT AU 9460428 A Based on WO 9419470; EP 667908 A1 Based on WO 9419470; US 5648332 A Based on WO 9419470; AU 686134 B Previous Publ. AU 9460428, Based on WO 9419470; CA 2134083 C Based on WO 9419470
PRAI JP 1993-179062 19930720; JP 1993-31501 19930222
AB WO 9419470 A UPAB: 19950705
Compsn. for treating or preventing autoimmune disease comprises a soluble **T cell receptor** alpha chain (I), produced by a suppressor T cell, and a carrier. Alternatively, (I) is replaced by a chimaeric protein (Ia) consisting of (I) and a constant region (II) of an

immunoglobulin.

USE/ADVANTAGE - (I) is used to treat or prevent diseases associated with a wide range of autoantigens, irrespective of the specificity of the suppressor cell from which it is derived. Typical conditions include insulin-dependent diabetes mellitus (DDM); systemic lupus erythematosus; rheumatoid arthritis; Graves disease; multiple sclerosis; chronic active hepatitis etc. Since (I) acts specifically to prevent localised, anomolous stimulation of the **immune** system, it has fewer side effects than conventional **immunosuppressant** treatments.

Dwg.2/4

L25 ANSWER 19 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1993-368712 [46] WPIDS
CR 2001-101695 [08]
DNC C1993-163648
TI Recombinant prodn. of **immunoglobulin**-like domains - useful for in vitro mutagenesis studies and in passive immunisation to treat disease.
DC B04 D16
IN KIM, J; WARD, E S
PA (TEXA) UNIV TEXAS SYSTEM
CYC 43
PI WO 9322332 A2 19931111 (199346)* EN 144p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR CA CH CZ DE DK ES FI GB HU JP KP KR LK LU MG MN MW NL NO NZ PL PT RO RU SD SE SK UA US VN
AU 9341167 A 19931129 (199411)
EP 640094 A1 19950301 (199513) EN
R: CH DE FR GB IT LI
WO 9322332 A3 19940217 (199515)
ADT WO 9322332 A2 WO 1993-US3895 19930426; AU 9341167 A AU 1993-41167 19930426; EP 640094 A1 EP 1993-910800 19930426, WO 1993-US3895 19930426; WO 9322332 A3 WO 1993-US3895 19930426
FDT AU 9341167 A Based on WO 9322332; EP 640094 A1 Based on WO 9322332
PRAI US 1992-963333 19921019; US 1992-873930 19920424
AB WO 9322332 A UPAB: 20010224
Novel recombinant vector comprises an inductible promoter sequence (P), a leader sequence (L) operatively positioned downstream of (P) and a DNA segment encoding an **immunoglobulin**-like domain (I) operatively positioned downstream of (L),. The vector resulting in secretion of (I) following incorporation into a Gram negative bacterium.

The vector pref. also comprises a tag sequence positioned downstream of the DNA segment encoding (I) and in the same reading frame. The tag is pref. myc or his.

Also claimed are: a recombinant antibody constant domain (Ia) obtainable from a recombinant bacterium and purified relative to its natural state; an antibody with a decreased biological half life, a method for producing a recombinant protein with modified biological stability or half life comprising preparing a **fusion protein** in which the **protein** is linked to a native or mutant antibody Fc-hinge domain or a native or mutant antibody Fc domain; and a method for producing an antibody with a decreased biological half life by preparing an antibody in which the Fc-hinge domain comprises an aminoacid mutation which results in impaired SpA binding.

(I) comprises an antibody constant domain ie (Ia), such as an Fc-hinge, Fe, a CH2-hinge or a CH3 domain. Pref. hosts are E.coli, Serratia marcescens or salmonella typhimurium.

USE - The invention facilitates the large scale prodn. of (I), including those derived from human sources, with a wide variety of applicns. E.g, (I) may be used in in vitro mutagenesis studies and in high resolution structural analyses, such as NMR and X-ray crystallography.

Recombinant Valpha, Vbeta, Vdelta, Vgamma, single chain ValphaVbeta fragments, domains or subfragments may be used for mapping the **TCR** residues which are functionally important in binding peptide-**MHC** complexes. Mutants binding with higher affinity to peptide-**MHC** complexes may be selected for and used eg., in therapy of autoimmune disease as blocking reagents. (I) may also be used in immunisation protocols for the generation of anti-clonotypc antibodies, useful e.g, in passive immunisation for treatment of disease, such as T cell leukaemias. The Fc-hinge or Fc domans may be linked to other proteins or drugs for immunotherapy. Chimaeric proteins or drugs with prolonged half lives may be produced.
Dwg.0/17

L25 ANSWER 20 OF 20 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1993-182537 [22] WPIDS
DNC C1993-080885
TI Chimeric mol. comprising **MHC** and **immunoglobulin** constant region - binds to **T cell receptors**, useful for treating auto **immune** diseases e.g. rheumatoid arthritis and multiple sclerosis.
DC B04 D16
IN ARMSTRONG, R J; SELICK, H E
PA (ANER-N) ANERGEN INC
CYC 36
PI WO 9310220 A1 19930527 (199322)* EN 40p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA SE
W: AT AU BB BG BR CA CH CS DE DK ES FI GB HU JP KP KR LK LU MG MN MW NL NO PL RO RU SD SE
AU 9332205 A 19930615 (199340)
ADT WO 9310220 A1 WO 1992-US10030 19921118; AU 9332205 A AU 1993-32205 19921118
FDT AU 9332205 A Based on WO 9310220
PRAI US 1991-795897 19911119
AB WO 9310220 A UPAB: 19931115
The compsn. comprises a chimeric mol. which selectively binds a **T cell receptor**. The chimeric mol. comprises a **MHC** component linked to an **immunoglobulin** constant region component, where the **MHC** component comprises an antigen binding pocket bound to an autoantigenic peptide. The compsn. may further comprise a protease (e.g. Factor Xa or collagenase) recognition site between the **MHC** component and the **immunoglobulin** constant region component.

Also claimed are: (1) a recombinant expression cassette comprising a promoter sequence operably linked to a first nucleotide sequence encoding a **MHC** protein chain and a second nucleotide sequence encoding an immunoglobin constant region protein chain; and (2) a method purifying a soluble **MHC** mol. comprising (a) containing an affinity column with a compsn. comprising a chimeric molecule having a **MHC** component linked to an **immunoglobulin** constant region component via an amino acid sequence having a protease recognition site, where the affinity column specifically binds the **immunoglobulin** constant region, and (v) treating the column with a protease capable of selectively cleaving the **chimeric protein** at the protease recognition site, thereby releasing the **MHC** component from the column. The affinity column is pref. a protein A/G-Sepharose (RTM) column.

USE/ADVANTAGE - The **chimeric proteins** are capable of binding a **T cell receptor** through the **MHC** component while the **immunoglobulin** component retains normal effector functions and provides the **chimeric proteins** with an extended serum half-life and other advantages.

only Constant region

They can be used for treating autoimmune diseases such as rheumatoid arthritis and multiple sclerosis (claimed). They can also be used for e.g. purifying **MHC** molecules, T cell typing, diagnosis and imaging and producing and purifying anti-**MHC** antibodies.
Dwg.0/5b